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CONGENITAL MUSCULAR HYPERTROPHY

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PHILADELPHIA

In 1934 DeLange [1] reported a syndrome, occurring in infants, characterized by congenital muscular hypertrophy, extrapyramidal disturbances and mental deficiency. She described three cases which had come directly under her observation and cited one case which had been reported nearly a half-century before by Bruck.[2] With the possible exception of one other case, which will be referred to later (Schiff and Balint [3]), these four cases are the only instances of this syndrome which we have found reported in the literature. We are presenting an additional case, with certain studies on the metabolism of the patient.

REPORT OF CASE

History.—A Negro boy was delivered at the Philadelphia General Hospital spontaneously and without injury at term in July 1933. The mother, a low grade moron, was only 14 years of age. The father of the patient was also the father of the child's mother. The weight of the child at birth was 5 pounds (2,268 Gm.). It was noted that his musculature was excessively developed. He was breast fed, gained weight steadily and was discharged in the care of the mother. He was readmitted to the Philadelphia General Hospital at 2½ months of age, because of vomiting, undernutrition and a profuse nasal discharge. The muscular hypertrophy was again noted, and a number of studies, including biopsies of the muscle, were made. After his discharge from the Philadelphia General Hospital, the child was admitted to the Hospital of the University of Pennsylvania and remained under observation from March 1934 until July 1935.

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1. DeLange, C.: Congenital Hypertrophy of the Muscles, Extrapyramidal Motor Disturbances and Mental Deficiency: A Clinical Entity, Am. J. Dis. Child. **48**:243-268 (Aug.) 1934.

2. Bruck, F.: Ueber einen Fall von congenitaler Makroglossie combiniert mit allgemeiner wahrer Muskelhypertrophie, Deutsche med. Wchnschr. **15**:229, 1889.

3. Schiff, E., and Balint, A.: Ueber Kreatin- und Kreatininausscheidung beim Säugling, Arch. f. Kinderh. **69**:439-450, 1921.

Physical Examination.—Physical examination when the child was 7 months old disclosed several features of unusual interest. He displayed the "athlete or wrestler habitus" described by Bruck,[2] i. e., a short, thick neck, broad shoulders, a deep chest and pronounced muscular development (figure, *A*). The hypertrophy of the muscles was symmetrical and was most prominent in the extremities and the shoulder girdles. The muscles were felt immediately beneath the skin as extremely firm, rigid bands. Although they were markedly hypertonic, the hypertonicity seemed to be distributed equally, since opposing groups functioned in a normal manner. There was a slight but definite resistance to passive movement.

The skin was slightly thick, dry, shiny and tense over the entire body except on the dorsa of the wrists, hands and feet, where it was wrinkled and rough. Sweating seemed to be definitely diminished. There was ubiquitous sparseness of subcutaneous tissue. The superficial veins were prominent, simulating the prominent subcutaneous veins in the aged. The superficial lymph nodes were greatly enlarged, the palpable nodes varying from the size of a pea to that of an almond, and were firm, discrete and not tender. The cervical nodes were larger than those of either the axillary or the inguinal group.

The head was asymmetrical, being flattened posteriorly and to the left; the parietal bones were prominent (figure, *B*). Consequently, the anteroposterior diameter of the head was shortened and the biparietal diameter lengthened. The anterior fontanel was open, measuring 3 by 3 cm. The sutures were closed. Craniotabes was absent. The hair line was high anteriorly; the hair was coarse, dry and abundant. The auricles were large and thick. A small amount of pus was draining from each ear, and small perforations were present in each drum. There were marked bilateral exophthalmos and slight lagophthalmos. Extraocular movements were normal. The pupils were equal and reacted promptly to direct and consensual light. Ophthalmoscopic examination, performed with the child under the influence of chlorbutanol, revealed clear media, well defined disks and normal vessels. The nose was broad and flat and the bridge depressed. There was moderate congestion of the nasal mucous membrane, from which exuded a thin, watery discharge. The mouth was wide and the lips thick. The cheeks were slightly sunken, giving the impression that the facial muscles were not as hypertrophied as the muscles of the trunk and limbs. The tongue was large, broad and clean, protruding between the lips. Drooling of saliva was a common occurrence. Dentition had not developed. The pharynx was normal. The palatine tonsils were small. Withal, the face simulated that of an aged person. This was due largely to the exophthalmos, prominent malar tuberosities, sunken cheeks, wide mouth and narrow mandible.

There was moderate swelling on each side of the short, thick, muscular neck, owing to cervical adenopathy. The sternomastoid muscles were unusually prominent. There were slight retraction of the head and slight rigidity of the neck, but these features were not as pronounced as in DeLange's cases. The chest was well proportioned and exceptionally muscular. The cardiac rate was somewhat elevated (140 beats per minute when the infant was admitted), but otherwise the heart was normal. The blood pressure was 90 mm. of mercury systolic and 64 diastolic. The child was pot bellied, and the abdomen was markedly distended; the tendinous inscriptions of the rectus abdominis muscles, the linea alba and the linea semilunaris were well outlined. A small umbilical hernia was observed. The abdominal percussion note was tympanitic. The edge of the liver was palpable just below the right costal margin. The spleen was not felt. The external genitalia were well developed and unusually large, the penis possessing a redundant prepuce. Both testes had descended into the scrotum. Examination

of the anus disclosed marked hypertrophy of the external sphincter, which was visible as a thickened ring about the anal orifice. The tone of the sphincter was firm. Rectal examination gave negative results. At the lower end of the spine, over the sacrum, a slight indentation of the skin was noted. The hands and feet, including the toes and fingers, were broad and abnormally large.

Neurologic examination disclosed generalized muscular hypertonicity, slight resistance to passive movement, slight retraction of the head and slight rigidity

The patient at the age of 12 months. *A* shows the muscular development; *B*, the shape of the head; *C*, the patient suspended on two index fingers (the other fingers encircled the wrists as a precaution and did not support any of the weight), and *D*, the facies and the large hands and feet. The child sat only with support.

of the neck. There were periods of complete quiescence alternating with periods when the child, lying in a supine position, raised the trunk from the bed in a position simulating that in opisthotonos. He was unable to sit up without support at the age of 9 months, and when he was supported in a sitting posture the head was thrown back, so that if released he fell backward. There was a marked delay in the development of equilibrium. The abdominal, cremasteric and deep tendon reflexes were present and were somewhat hyperactive. There was a Babinski sign on each side. The nerves and muscles of the upper and lower extremities were tested with faradic and galvanic currents, and the reactions were found to be normal. There was no evidence of tetany, myotonia or degeneration.

The strength of the child was great when compared with that of normal children. He possessed an unusually strong grasp and frequently could be induced to hang unsupported from one's fingers, showing no signs of fatigue for sixty seconds or more (figure, *C*). However, a genuine grasp reflex could not be demonstrated.

Routine laboratory studies showed nothing abnormal except the presence of mild secondary anemia. The tuberculin test gave negative results with 1 mg. of old tuberculin. The Wassermann reaction of the blood, tested on three occasions, was negative with three antigens. The mother's Wassermann reaction, tested on one occasion, was negative. A Wassermann test of the father's blood could not be obtained. Examination of the cerebrospinal fluid yielded 5 cells per cubic millimeter, 38.5 mg. of total protein per hundred cubic centimeters, a negative Wassermann reaction and a colloidal gold curve of 0001110000.

Biopsies of the deltoid and gastrocnemius muscles, made at the Philadelphia General Hospital,[4] showed the individual fibers to be normal in length and diameter and their nuclei to be normal in size, shape and number. No evidence of degeneration, fibrous or fatty replacement or inflammation was present in any of the sections. A biopsy of a lymph node obtained from the right inguinal region revealed simple hyperplasia of the lymphoid tissue. Histologic sections of the skin disclosed atrophy, poorly developed papillae and infrequent capillary loops.

Roentgenograms of the skull, taken at the age of 8 months and again at 21 months, revealed no abnormality. Flat plates of the abdomen revealed no unusual masses. Because of the enlargement of the abdomen an enema of barium sulfate was given. The colon was found to be normal except in the region of the cecum, where an annular constriction at the level of the ileocecal valve, suggestive of a congenital band, was noted. An intravenous urogram (with 5 cc. of "diodrast"), made when the child was 9 months of age, disclosed normally functioning kidneys. The outlines of the renal pelves on both sides appeared normal, and no adrenal masses were suggested. The only roentgenographic finding of possible significance was a slight posterior displacement of the trachea, which may have been evidence of an enlarged thymus.

Growth and Development.—The child was underweight at birth (2,270 Gm.) and at the age of 7 months (6,180 Gm.), when he was first seen in the university hospital. He gained weight steadily with the usual dietary measures, weighing 9,740 Gm. at the age of 12 months and 13,630 Gm. at 22 months. The length of the body (crown-heel) was 70 cm. at 10 months and 89 cm. at 22 months.

Dentition was somewhat delayed, the lower medial incisors appearing at the age of 10 months. The child was unable to sit alone without support until he

4. The authorities of the Philadelphia General Hospital supplied the report of these examinations.

was 12 months of age; at the age of 16 months he stood in his crib without support, and at 18 months he began to walk. He was unable to talk at 22 months.

Mental development was retarded. According to tests with the Gesell method when his chronological age was 13.5 months, his mental age was 7 months. A second test, performed when the patient was 15 months old, disclosed that his mental age was 9.5 months. At the age of 17 months roentgenograms showed nothing abnormal in the appearance of the centers of ossification or in the epiphyses of the left wrist, elbow and knee except evidence of old healed mild rickets.

Results of Special Studies.—Special studies were directed chiefly to the measurement of the various components of the blood serum and of the excretion of creatine and creatinine in the urine and to the estimation of the total metabolism by means of the insensible perspiration.

Serum: The analyses of the serum are given in table 1. The concentrations of potassium, inorganic phosphate and phosphatase were particularly noteworthy. The concentration of potassium was, on one occasion, approximately 25 per cent

TABLE 1.—*Analyses of the Serum*

Date	Potassium, mEq. per Liter	Calcium, mEq. per Liter	Protein, Gm. per 100 Cc.	Inorganic Phosphorus, Mg. per 100 Cc.	Cholesterol, Mg. per 100 Cc.	Sugar, Mg. per 100 Cc.	Urea Nitrogen, Mg. per 100 Cc.	Creatine, Mg. per 100 Cc.	Phosphatase, Units per 100 Cc.
3/24/34	...	5.5	...	8.4	190.0	.....	12.0	1.2	....
5/ 8/34	5.5	6.6	6.1	7.3	147.0	111.0	11.0	1.1	....
10/15/34	...	...	...	5.8	.....	.....	....	...	49.0
1/24/35	4.6	5.2	6.7	5.7	147.0	.....	....	1.3	51.0

Date	Total Base, mEq. per Liter	Sodium, mEq. per Liter	Magnesium, mEq. per Liter	Chlorine, mEq. per Liter	Carbon Dioxide, Cc. per 1,000 Liters	Nonprotein Nitrogen, Mg. per 100 Cc.	Total Phosphorus, Mg. per 100 Cc.	Ester Phosphorus, Mg. per 100 Cc.	Lipoid Phosphorus, Mg. per 100 Cc.
1/24/35	143.5	132.3	1.7	109.0	19.0	20.0	12.6	0.1	7.0

above the upper limit obtained in this laboratory for the potassium concentration of serum of normal adults (from 3.8 to 4.3 milliequivalents per liter). The concentration of inorganic phosphate, as shown in two analyses, was greater than that for normal infants from 6 to 18 months of age (from 5 to 6 mg. per 100 cubic centimeters), as reported by Stearns and Warweg.[5] The remaining phosphorus fractions, however, were within the normal limits. Kay [6] has shown that in infants the serum phosphatase content ranges from 17 to 34 units per hundred cubic centimeters. This patient at the age of 14½ months had a serum phosphatase content of 49 units and at the age of 17 months of 51 units.

Total Metabolism: In order to obtain an estimate of the total metabolism of the patient, the insensible perspiration was measured. The insensible loss

5. Stearns, G., and Warweg, E.: Studies of Phosphorus of Blood: I. The Partition of Phosphorus in Whole Blood and Serum, the Serum Calcium and Plasma Phosphatase from Birth to Maturity, J. Biol. Chem. **102**:749-765, 1933; II. The Partition of Phosphorus in Blood in Relation to the Corpuscle Volume, J. Clin. Investigation **13**:411-418, 1933.

6. Kay, H. D.: Plasma Phosphates: I. Method of Determination; Some Properties of the Enzyme, J. Biol. Chem. **89**:235-247, 1930.

of weight was found to be, on the average, 7.6 Gm. per hour at the age of 10 months, which would indicate, according to Levine and Marples'[7] data, a heat production of approximately 395 calories per day. The normal heat production for a boy of the patient's age and weight was estimated as 450 calories per day, so that his metabolism was calculated to be approximately 12 per cent less than normal and probably within normal limits.

Urine: The quantities of creatine and creatinine excreted in the urine during twenty-four hour periods from the time the patient was 8½ until he was 22 months of age are given in table 2. The excretion of total creatinine was determined when he was on a creatine-free diet with a normal, low or high protein content, on a normal diet with the addition of amino-acetic acid and on a normal diet with the addition of creatine. It may be seen that the coefficients for creatine nitrogen and creatinine nitrogen were both greatly increased as compared with the values for normal children of corresponding ages (table 2) collected from the literature.[8] The excretion of creatine nitrogen by this patient when he was on an ordinary ward diet was from 39 to 46 per cent of the total excretion of creatinine nitrogen. With a low protein diet, the excretion of creatine nitrogen was reduced to 28 per cent of the total creatinine nitrogen. With a high protein diet the excretion of both creatinine nitrogen and creatine nitrogen was increased, and the creatine nitrogen was 51 per cent of the total creatinine nitrogen. The addition of amino-acetic acid to the diet further augmented the excretion of both creatine and creatinine. The ingestion of 0.5 Gm. of creatine hydrate (141 mg. of creatine nitrogen) caused an increase in the excretion of creatine, approximately all the creatine hydrate ingested being excreted within forty-eight hours.

Observations.—During the patient's long stay in the hospital, certain noteworthy facts were evident. The original infection of the nasopharynx, ears and cervical nodes abated and then showed an occasional recrudescence; it did not clear up entirely until after an adenoidectomy was performed in February 1935. Although the child was unable to sit or stand until he was well into his second year, it is reasonable to consider that this retardation resulted from mental deficiency. Within the limits of his mental capacity he was always alert, and he gave many exhibitions of temper. As soon as he achieved equilibrium he became as active as a normal child and could never be left without the restraint of a crib or exercise pen. At no time was it possible to predicate the existence of any definite disease of the endocrine system, including calcification of the pineal body.

COMMENT

The syndrome of congenital muscular hypertrophy, extrapyramidal motor disturbances and mental deficiency seems to be a clinical entity. It should be noted, however, that any of the main features of the syndrome may be subject to considerable variation. In DeLange's[1] cases, judging from the illustrations in her paper, the degree of muscular hypertrophy was not as striking as in Bruck's case or as in the

7. Levine, S. Z., and Marples, E.: The Insensible Perspiration in Infancy and in Childhood: III. Basal Metabolism and Basal Insensible Perspiration of the Normal Infant; a Statistical Study of Reliability and of Correlation, Am. J. Dis. Child. **40**:269-284 (Aug.) 1930.

8. Hunter, A.: Creatine and Creatinine, in Monographs on Biochemistry, London, Longmans, Green & Co., 1928, p. 186.

TABLE 2.—*Statistics Concerning the Creatinine Content*

Date	Age, Months	Weight, Gm.	Remarks	Data on Hour Collection of Urine: Total Nitrogen, Gm.	Creatinine Nitrogen, Mg.	Creatine as Creatinine N., Mg.	Creatinine Nitrogen Coefficient	Creatine Nitrogen Coefficient	Total Creatinine Nitrogen Coefficient
4/17/34	8½	7.2	With ward diet	....	66.4	57.1	9.2	7.9	17.1
4/20/34	8⅔	7.4	With ward diet	....	63.1	46.4	8.5	6.3	14.8
5/ 9/34	9⅓	8.1	With ward diet	....	66.4	55.3	8.2	6.8	15.0
2/28/35	19	14.1	With ward diet	....	116.1	73.5	8.2	5.2	13.4
4/22/35	21	13.2	With ward diet: 1,500 calories, 46 Gm. of protein, daily	4.86	112.8	81.2	8.5	6.2	14.7
4/29/35	21	13.6	With a low protein diet; 1,500 calories, 15 Gm. of protein daily for 5 days previous	1.71	85.3	33.0	6.3	2.4	8.7
5/ 5/35	21	13.6	With a high protein diet; 1,500 calories, 85 Gm. of protein, daily for 7 days previous	6.87	124.3	126.6	9.1	9.3	18.4
5/20/35	21⅔	13.7	1,500 calories; 50 Gm. of protein + 5 Gm. of amino-acetic acid, daily for 6 days previous	4.43	140.0	145.4	10.2	10.6	20.8
*5/30/35	22	13.6	1,500 calories; 50 Gm. protein daily; 0.5 Gm. of creatine hydrate (141 Mg. of creatine nitrogen), at beginning of 48 hour collection	5.63	123.6	162.0	...	...	21.0 (15.8†)
5/31/35	..	....		5.63	123.6	162.0	...	...	21.0 (15.8†)
Authors			Normal Values for the Same Age Group‡						
Denis and Kramer [12]	13	9.6	With a high protein diet	3.2	37.1	32.6	3.9	3.4	7.3
Denis and Kramer [12]	13	9.6	With a low protein diet	1.7	38.2	20.0	4.0	2.1	6.1
Gamble and Goldschmidt§	8	5.4	0.96 Gm. of nitrogen ingested	0.50	20.8	4.5	3.9	0.8	4.7
Gamble and Goldschmidt§	10	6.5	3.20 Gm. of nitrogen ingested	1.89	28.9	21.9	4.5	3.4	7.9
Gamble and Goldschmidt§	14	6.5	1.12 Gm. of nitrogen ingested	0.84	26.0	23.0	4.0	3.5	7.5
Gamble and Goldschmidt§	14	6.8	5.76 Gm. of nitrogen ingested	5.08	30.1	46.0	4.4	6.8	11.2

* Value for the 48 hour collection, divided by 2.
† Total creatinine nitrogen coefficient corrected to allow for the 141 mg. of creatine nitrogen ingested.
‡ Hunter.[8]
§ Gamble, J. L., and Goldschmidt, S.: A Study of Creatinuria in Infants: I. Relation of Creatinuria to Acidosis; the Elimination of Ingested Creatine and Creatinine, J. Biol. Chem. **40**: 199, 1919; II. Relation of Protein Intake to Urinary Creatine, ibid. **40**: 215, 1919.

case described in this report. On the other hand, the extrapyramidal motor disturbances were more marked in DeLange's cases. In our case the only evidences of extrapyramidal disturbances were the hypertonicity, the slight resistance to passive movement, the slight rigidity of the neck and the tendency to assume the position of opisthotonos. With the exception of the hypertonicity, these features gradually disappeared during the months that the child remained under observation.

The pathologic process responsible for the disturbance in the extrapyramidal system is uncertain. In two of the four reported cases the brain was examined at necropsy. According to Bruck, the brain of his patient appeared normal macroscopically and microscopically. DeLange, on the other hand, observed malformation of the corpus striatum and widespread porencephaly in a case in which the signs of extrapyramidal motor disturbance had been pronounced. Bruck reported his case at a time when disturbances of the paleokinetic system were not recognized, and it is probable that a detailed examination of the corpus striatum was not made.

The four patients whose cases were previously reported died during the first twenty months of life. Two of DeLange's patients apparently died as a result of the disease. Bruck's patient and one of DeLange's died of pneumonia. The patient whose case is reported in this paper has lived longer than any of the others. After his discharge from the hospital our patient was admitted to an institution for the feebleminded, and he was reported in January 1936 to be thriving, at the age of 2½ years, without any change in his muscular overdevelopment.

The syndrome of congenital muscular hypertrophy, extrapyramidal motor disturbances and mental deficiency is not likely to be confused with any other disease of infancy or childhood. Other types of congenital muscular hypertrophy, affecting one half of the body, one extremity, etc., have been reported (Kitaigorodskaja[9]), but they are quite different from the "wrestler habitus," with its symmetrical hypertrophy of the entire voluntary musculature. The presence of extrapyramidal motor disturbances and mental deficiency facilitates, and is at present considered an essential feature for, the diagnosis of this condition.

The differentiation of this syndrome from myotonia congenita (Thomsen's disease) may be made on the basis of the age at which it appears, the clinical picture, electrical stimulation of the voluntary musculature and biopsy of muscles. In myotonia congenita an increase in the tonicity of the muscles is associated with difficulty in the initiation

9. Kitaigorodskaja, O. D.: Angeborene Hypertrophie im Kindesalter, Jahrb. f. Kinderh. **125**:38-89, 1929.

and cessation of movements, features usually developing at about the period of puberty. Moreover, in that disease the histologic picture obtained by biopsy of muscles, and the reaction of the muscles to electrical stimulation show special characteristics. In congenital muscular hypertrophy, on the other hand, hypertonia associated with massive hypertrophy of the musculature of the body is present at birth, there is no difficulty in the initiation or cessation of movements, the reactions to electrical stimulation are normal and biopsies show normal muscles.

The syndrome of congenital muscular hypertrophy appears to be easily differentiated from the pseudohypertrophic type of muscular dystrophy. The latter condition is invariably accompanied by muscular weakness and exhibits histologic degenerative changes in the muscle fibers.

In adults a form of symmetrical muscular hypertrophy termed hypertrophica musculorum vera has been described by Spiller.[10] This condition is associated with pronounced weakness of the muscles without microscopic evidence of degeneration in the muscle fibers. Its relation, if any, to congenital muscular hypertrophy is not known.

The high total creatinine nitrogen coefficient observed in the case reported in this paper is of unusual interest. Children normally excrete creatine as well as creatinine in the urine, the creatinuria disappearing at puberty. In patients with muscular dystrophy creatinuria occurs, but the amount excreted is usually less than that found in the urine of normal children. We have encountered in the literature only one report of a case in which the excretion of creatine and creatinine was similar to that observed in this case. In 1921, Schiff and Balint,[3] while studying the excretion of creatine and creatinine in the urine of infants with various diseases of the muscular system, observed one patient with a high total creatinine coefficient. The value observed was approximately the same as that noted in our patient. Their patient was a 7 month old infant who showed pronounced muscular hypertrophy, spastic extremities, exaggerated reflexes, a Babinski sign and idiocy. Their diagnosis was encephalitis. Despite the briefness of their description, they reported findings which suggest that their case might belong in the group under discussion. The daily excretion of creatine and creatinine has been shown by Shaffer [11] to be roughly related to muscle mass. It appears, therefore, that the high values observed in their patient are consistent with the generalized muscular hypertrophy.

Denis and Kramer [12] found that in normal children the amount of creatine in the urine is directly dependent on the intake of protein,

10. Spiller, W. G.: The Relation of the Myopathies, Brain **36**:75-114, 1913.

11. Shaffer, P.: The Excretion of Kreatinin and Kreatin in Health and Disease, Am. J. Physiol. **23**:1-22, 1908.

12. Denis, W., and Kramer, J. G.: The Influence of Protein Intake on Creatine Excretion in Children, J. Biol. Chem. **30**:189-196, 1917.

being high when large quantities of protein are ingested and decreasing and in some cases disappearing when the child is fed a diet with an extremely low protein content. Harding and Gaebler [13] claimed: "Creatine is produced from protein either *in toto* or from a special fraction of it, is stored in the muscles, and is converted into creatinine. With the saturation of the muscles with creatine, any excess production will find its way into the urine, and provided the dietary protein is not reduced to such a low level that a condition of protein starvation occurs, the urinary creatine will appear as a waste product of exogenous origin." Our patient received the ordinary ward diet, containing from 45 to 50 Gm. of protein daily, until after the measurement of the excretion of total creatinine in the urine made on April 22, 1935. When the patient was placed on an isocaloric diet containing little protein (15 Gm. daily), the total creatinine nitrogen coefficient dropped considerably but never fell below the total creatinine nitrogen coefficient of normal children with an adequate protein intake. This decrease was chiefly in the creatine fraction. When the child was placed on an isocaloric diet with a high protein content (85 Gm. daily) the total creatinine nitrogen coefficient rose to a remarkably high level, approximately twice as high as that observed in normal children. In view of these findings, it appears that in this patient the metabolism of creatine was influenced to an unusual extent by the amount of protein ingested.

The increase in the concentration of potassium and inorganic phosphate in the serum, as well as the increase in the excretion of creatine and creatinine in the urine, may be related to the increase in muscular development and metabolism, since the concentrations of potassium and inorganic phosphate are normally higher in muscle tissue than in blood serum. Studies in the literature [14] indicate that changes in the inorganic phosphate concentration in the serum may occur during various physiologic activities involving the muscles. The experiments of Wilder [15] may also be cited, in which it was shown that in rachitic rats the high concentration of inorganic phosphate in the plasma was caused by destruction of body protoplasm.

The occurrence of a high phosphatase content in the serum of the patient whose case we have reported is not explained. There was no evidence of disease of the bones or the liver in the clinical observations or roentgenograms.

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13. Harding, V. C., and Gaebler, O. H.: On the Constancy of the Creatine-Creatinine Excretion in Children on a High Protein Diet, J. Biol. Chem. **54**: 579-587, 1922.

14. Havard, R. E., and Reay, J. A.: The Influence of Exercise on the Inorganic Phosphates of the Blood and Urine, J. Physiol. **61**:35-48, 1926.

15. Wilder, G. S.: The Tetany of Fasting in Experimental Rickets, J. Biol. Chem. **81**:65-72, 1929.

CONCLUSIONS

The syndrome of congenital muscular hypertrophy, extrapyramidal motor disturbances and mental deficiency appears to be a separate clinical entity. In addition to the case presented in this paper, only four or possibly five other cases have been reported in the literature.

In our case there were noted an abnormally high excretion of creatine and creatinine in the urine and an exaggerated response in the creatine excretion to variations in the amount of protein ingested. The concentrations of potassium, inorganic phosphate and phosphatase in the blood serum were high. The greatly hypertrophied voluntary muscles were normal histologically and in their reaction to electrical stimulation.

NOTE.—Just after this article was submitted for publication, a report by Debre and Semelaigne of two cases of diffuse muscular hypertrophy in infants appeared.[16] It seems to us that these cases differed materially from the one here reported. The muscular hypertrophy in our case was accompanied by pronounced muscular strength, not weakness, and the growth after slight retardation in the first few months was entirely normal. Our patient was mentally retarded but not sluggish, as they described their patients. The question of endocrine disturbance was carefully considered in our case, and the consensus of many persons was that evidence of such disturbance was entirely lacking.

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16. Debré, Robert, and Semelaigne, G.: Syndrome of Diffuse Muscular Hypertrophy in Infants Causing Athletic Appearance: Its Connection with Congenital Myxedema, Am. J. Dis. Child. **50**:1351 (Dec.) 1935.

SERUM CHOLESTEROL VALUES FOR CHILDREN

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The purpose of this report is a statistical evaluation of the free and total cholesterol values found for three groups of patients at the Seaside Hospital from June to September 1935. These patients, ranging in age from the neonatal period to 12 years, were about equally divided between the sexes. The pathologic conditions represented were (1) infection of tonsils and adenoids, (2) rheumatic fever, including rheumatic carditis, and (3) miscellaneous acute and chronic infections, including osteomyelitis, pleurisy, rickets, diabetes, acute glomerulonephritis, asthma, residual poliomyelitis, malnutrition, eczema, pylorospasm, torticollis and bronchiectasis.

Little work has been done in the determination of values for free and combined cholesterol in the blood of children. Recently Sperry [1] reported free and total cholesterol values for heparinized blood plasma of children in the neonatal period. The range was from 25 to 61 mg. and from 71 to 190 mg. per hundred cubic centimeters for free and for total cholesterol, respectively. On the other hand, many reports have been published concerning the values for adults, some of which will be reviewed briefly. In 1927, Gardner and Gainesborough [2] reported plasma cholesterol values for twenty-one normal women and twenty-two normal men.

The means and standard deviations were as follows:

	Total Cholesterol, Mg. per 100 Cc.		Free Cholesterol, Mg. per 100 Cc.
Women	153 ± 33	Women	54 ± 17
Men	169 ± 41	Men	50 ± 21

In 1933, Man and Peters [3] reported a total cholesterol value of 207 mg.

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1. Sperry, W. M.: Cholesterol of Blood Plasma in Neonatal Period, Am. J. Dis. Child. **51**:84 (Jan.) 1936.

2. Gardner, J. A., and Gainesborough, A.: A Study of Normal Cholesterol Values, Biochem. J. **22**:1048 (Nov.) 1927.

3. Man, E. B., and Peters, J. P.: Plasma Cholesterol Values of Normal Adults, J. Biol. Chem. **101**:658 (Aug.) 1933.

± 29 for twelve normal patients of both sexes. Page and his associates [4] in 1935 studied the plasma cholesterol values of sixty-six normal men ranging from 20 to 90 years of age and obtained a mean value of 232 mg. ± 62 for total cholesterol and of 82 mg. ± 17 for free cholesterol. These authors concluded that variations in age from 20 to 90 years have no determinable influence on either the amount or the composition of plasma lipids. Sperry,[5] in a study of ninety-one healthy adult subjects, found an average value for total cholesterol of 209.8 mg. and a mean percentage of free cholesterol of 26.9 ± 1.4 (standard deviation).

Boyd,[6] investigating diurnal variations in the blood lipid content, concluded that normal persons under normal conditions of life exhibit but slight variations in the concentration of plasma lipids. He found that the standard deviation per person per day in the value for free and for ester cholesterol comprised on the average 6.5 per cent and 7.2 per cent, respectively, of the mean for the day. His mean values for eight subjects were 177 mg. per hundred cubic centimeters for total and 51 mg. for free cholesterol. In 1933 Okey and Stewart [7] studied the effect of diets with a low, moderate and high cholesterol content on four women and found that the mean values for a month during which a diet with a high cholesterol content was given were consistently somewhat higher for total and free cholesterol than they were when the control diet was given. Determinations were done on blood plasma. Cantarow,[8] in his review of the present status of cholesterol investigation, noted that the blood cholesterol concentration of normal persons is little changed by diurnal food consumption but is consistently somewhat higher when they are on a diet with a high fat content. He quoted such workers as McEachem and Gilman, who reported significant diurnal variations in plasma cholesterol values for the same persons, and Bruger and his associates, who could not find such diurnal variations. Bruger and Poindexter [9] noted that for nine different subjects the ingestion of from 500 to 1,000 cc. of water caused no appreciable change in the plasma cholesterol value from the value during fasting except in one instance, in which it fell. The previously

4. Page, I.; Kirk, E.; Lewis, W.; Thompson, W., and Van Slyke, D.: Plasma Lipids of Normal Men at Different Ages, J. Biol. Chem. **111**:613 (Nov.) 1935.

5. Sperry, W. M.: Relationship Between Total and Free Cholesterol in Human Serum, J. Biol. Chem. **114**:125 (May) 1936.

6. Boyd, E. M.: Diurnal Variations in Plasma Lipids, J. Biol. Chem. **110**:61 (June) 1935.

7. Okey, R., and Stewart, D.: Diet and Blood Cholesterol in Normal Women, J. Biol. Chem. **99**:717 (Feb.) 1933.

8. Cantarow, A.: Progress in Cholesterol Metabolism, Internat. Clin. **2**:237 (March) 1935.

9. Bruger, M., and Poindexter, C.: Effects of the Ingestion of Water and Urea on the Cholesterol Content of the Plasma, J. Biol. Chem. **101**:21 (June) 1933.

unpublished findings of Offenkrantz and Feraru (table 1), obtained in a study of the diurnal variations of the serum cholesterol concentration in male medical students, are further evidence of the lack of significant diurnal variations in cholesterol content in the same person and of the fact that a sample of blood for cholesterol analysis may be taken at any time of the day. Table 1 shows that the specimens taken during fasting show no significant variations as compared with specimens from the same person taken at a later hour.

Some of the cholesterol values which have been reported for patients with pathologic conditions similar to those of the patients we studied follow. Hartung and Bruger,[10] for thirty-three patients with rheumatoid arthritis, found a mean value for the total plasma cholesterol of 175.2 mg. per hundred cubic centimeters ± 39.5, which represents a definite decrease from the normal values obtained by them. An increasing number of investigators find hypocholesteremia accompany-

TABLE 1.—*Values for the Free and the Total Cholesterol in the Blood Serum of Male Medical Students, Showing a Lack of Diurnal Variation*

Case No.	Time of Collection of Specimen Taken During Fasting	Free Cholesterol	Total Cholesterol	Time of Collection of Second Specimen	Free Cholesterol	Total Cholesterol
1	8:30 a. m.	74.1	225.3	12:00 m.	65.3	225.0
2	8:30 a. m.	46.4	149.0	12:00 m.	42.6	141.5
3	7:30 a. m.	54.0	165.3	3:00 p. m.	54.8	169.7
4	7:30 a. m.	62.2	222.2	3:00 p. m.	61.5	225.0
5	7:30 a. m.	48.7	147.1	3:00 p. m.	52.6	153.0
6	8:30 a. m.	51.7	163.6	11:00 a. m.	49.5	167.8
7	8:30 a. m.	52.9	159.8	11:00 a. m.	45.3	150.5
8	7:30 a. m.	60.9	216.0	7:30 p. m.	62.8	202.4
9	7:30 a. m.	65.2	225.7	7:30 p. m.	62.7	219.2
10	7:30 a. m.	56.6	198.9	7:30 p. m.	56.1	189.9

ing many types of infection. Okey and Boyden,[11] studying the cyclic variations of the plasma cholesterol concentration in women found that the common cold lowered the values significantly. McQuarrie and Stoesser[12] found a lowering of the cholesterol content and an elevation of the body temperature in patients with infection and induced fever. Boyd[13] studied twelve cases of infectious fever and found a fall in the ester and a slight rise in the free cholesterol concentration at the onset of the fever and a severe drop in both at the height of the fever. Lesne and his associates, quoted by Ashe and Bruger,[14]

10. Hartung, E. F., and Bruger, M.: Cholesterol Content of the Plasma in Arthritis, J. Lab. & Clin. Med. **20**:675 (April) 1935.

11. Okey, R., and Boyden, R. E.: Studies in the Metabolism of Women: III. Variations in the Lipid Content of the Blood with Relation to the Menstrual Cycle, J. Biol. Chem. **72**:261 (March) 1927.

12. McQuarrie, L., and Stoesser, A.: Influence of Acute Infections and Artificial Fever on Plasma Lipids, Proc. Soc. Exper. Biol. & Med. **29**:1281 (June) 1932.

13. Boyd, E. M.: The Lipopenia of Fever, Canad. M. A. J. **32**:500 (May) 1935.

14. Ashe, B., and Bruger, M.: The Cholesterol Content of the Plasma in Chronic Nephritis, Am. J. M. Sc. **186**:670 (Nov.) 1935.

noted hypocholesteremia in cases of severe acute nephritis, while Bennet found normal values in similar cases. Ashe and Bruger found a marked drop in the plasma cholesterol content in patients with marked cachexia and anemia. Bruger and Mosenthal [15] observed that there was no alteration in the plasma cholesterol concentration in diabetic patients after the injection of insulin.

EXPERIMENTAL METHOD

Blood was drawn by venipuncture into 15 cc. centrifuge tubes and was placed in a refrigerator within a half hour, the tubes being tightly stoppered. After twenty-four hours the clot was rimmed with a thin glass rod, and the sample was centrifugated for fifteen minutes at about 1,500 revolutions per minute. The serum was pipetted into centrifuge tubes and recentrifugated for five minutes to insure removal of cells. The free and the total cholesterol value were determined by the method of Schoenheimer and Sperry,[16] with the modification described by Fitz.[17] Instead of the cholesterol standard described by the latter, the ink standard devised by Shapiro was used.[18] Cholesterol present as ester (or combined cholesterol) was calculated by subtracting the free from the total cholesterol. The ratio of combined to free cholesterol, as employed by Schoenheimer and Sperry is used in this report. The desirability of using serum rather than oxalated plasma in cholesterol studies is shown by the recent work of Sperry and Schoenheimer,[19] who found that analysis of the latter gave significantly lower values for both total and free cholesterol.

The statistical procedures employed are as follows:

Arithmetical mean $(M) = G.A. + c$

Correction factor $(c) = \xi d/N$

Standard deviation of a single observation $(\sigma) = \sqrt{\frac{\xi d^2}{N} - c^2}$

Probable error of the mean $(P.E_m) = 0.6745 \times \sigma/\sqrt{N}$

Significance value $(S) = \frac{\text{Difference of means}}{\sigma_d \text{ of difference}}$

Standard deviation of a difference between means $(\sigma_d) = \sqrt{\left(\frac{\sigma_1}{N_1}\right)^2 + \left(\frac{\sigma_2}{N_2}\right)^2}$

G.A. = guessed average of a series
d = algebraic difference between G.A. and a single observation
ξd = algebraic sum of differences (d) for a series
N = number of determinations in a series.

15. Bruger, M., and Mosenthal, H.: The Immediate Response of the Plasma Cholesterol to the Injection of Insulin and Epinephrine in Humans, J. Clin. Investigation **13**:399 (May) 1934.

16. Schoenheimer, R., and Sperry, W. M.: A Micromethod for the Determination of Free and Combined Cholesteroi, J. Biol. Chem. **106**:745 (Sept.) 1934.

17. Fitz, F.: The Application of the Colorimeter to the Schoenheimer and Sperry Method for the Determination of Free and Combined Cholesterol, J. Biol. Chem. **109**:523 (May) 1935.

18. Shapiro, A.; Lerner, H., and Posen, E.: A Fixed Color Standard for Cholesterol Determinations, Proc. Soc. Exper. Biol. & Med. **32**:1300 (July) 1935.

19. Sperry, W. M., and Schoenheimer, R.: A Comparison of Serum, Heparinized Plasma and Oxalated Plasma with Regard to Cholesterol Content, J. Biol. Chem. **110**:655 (Aug.) 1935.

OBSERVATIONS

In any series of determinations there are often a certain number of values which fall beyond the furthest probable range of values for the group under study. The aberration may be due to an unrecognized factor operating only in those determinations, thus invalidating them for use in the series, or merely to an error in technic. It is permissible to cast out such determinations, indicating in each case the values that have been dropped.

The patients with involvement of tonsils and adenoids, who were otherwise "clinically normal," were selected at random from among

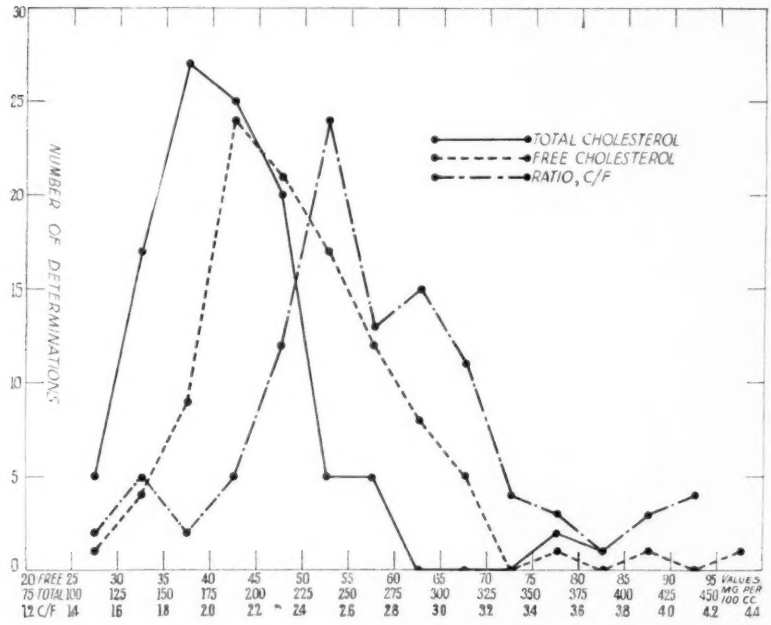

Chart 1.—Curves showing the frequency of values for the free and the total cholesterol and the ratio of combined to free cholesterol for the group with infection of tonsils and adenoids.

those scheduled for operation. The usual physical findings were hypertrophied tonsils and adenoids, with moderate cervical lymphadenitis. Prior to operation these patients showed no febrile reaction, and the urine collected preoperatively gave negative results on routine examination. The blood was drawn before breakfast, after a fast of twelve hours. There were fifty boys and fifty-seven girls, ranging in age from 3 to 12 years, and a single determination for each patient was made. Figure 1 shows a distribution curve for the values for free and total cholesterol and those for the ratio of combined to free

cholesterol obtained for this so-called normal group. Other than the terminal aberrations of all three curves, the most striking feature is a marked skewing to the right of the curve for free cholesterol. A comparable skewing to the right of the curve for the ratio of combined to free cholesterol cannot be interpreted, since the figures involved are dependent on two variables, the cholesterol values. A possible explanation of this phenomenon is found later in this report.

Table 2 contains the mean values and the statistical analysis for this group. The values obtained when the determinations for the boys and the girls were combined were 183.3 mg. per hundred cubic centimeters ± 46.8 for total cholesterol, 49.9 mg. ± 12.1 for free cholesterol and 2.67 ± 0.55 for the ratio of combined to free cholesterol. These can

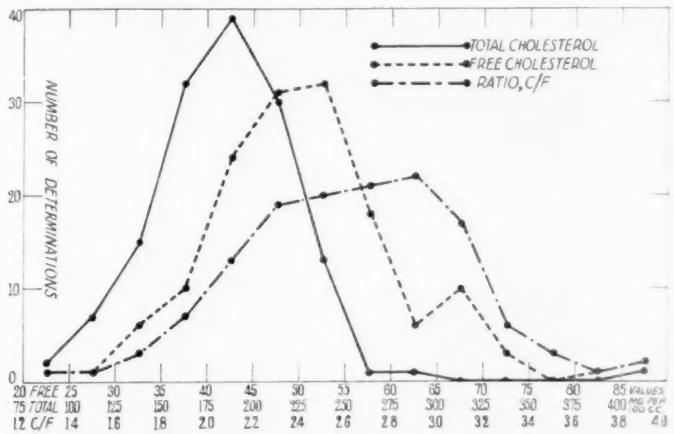

Chart 2.—Curves showing the frequency of values for the free and the total cholesterol and the ratio of combined to free cholesterol for the group with rheumatic fever.

be regarded as normal values, with which the findings for other groups may be compared. The standard deviations were less than 25 per cent of the means, and the probable errors of the means were less than 2 per cent of the respective means in each instance. The range in the ratio of combined to free cholesterol noted previously was somewhat greater than that found by Sperry [20] for normal children. The finding of a greater variability may have been due to the use of the colorimeter instead of the more sensitive photometer in the analytic procedure.

In the second group were sixty-five patients with rheumatic fever, for whom 140 determinations were performed. Blood was drawn at varying intervals during the day, at no set time with regard to eating or activity. Six determinations were performed for the same person in

20. Sperry, W. M.: Personal communication to the authors.

some instances, no determinations, however, being less than a week apart. There were large variations in the results of such repeated determinations for the same persons, the probable explanation of which, involving such factors as damage to the liver, congestion of other viscera

TABLE 2.—*Values for the Free and the Total Cholesterol and the Ratio of Combined to Free Cholesterol for All Groups of Patients*

	Number of Cases	Sex	Mean Value, Mg. per 100 Cc.	Standard Deviation	Probable Error of Mean	Significance Value
Patients with Infections of Tonsils and Adenoids ("Normal Group")*						
Free cholesterol	48	Boys	49.1	11.3		
	57	Girls	50.7	12.8		
	105	Both sexes	49.9	12.1	0.73	....
Total cholesterol	50	Boys	185.4	48.3		
	57	Girls	181.6	45.3		
	107	Both sexes	183.4	46.8	2.32	....
Ratio of combined to free cholesterol	48	Boys	2.83	0.54		
	55	Girls	2.54	0.56		
	103	Both sexes	2.67	0.548	0.036	....
Group with Rheumatic Fever						
Free cholesterol	70	Boys	50.2	8.6		
	71	Girls	50.2	9.4		
	141	Both sexes	50.2	9.1	0.51	0.12
Total cholesterol	70	Boys	184.3	32.8		
	71	Girls	183.2	35.2		
	141	Both sexes	183.7	33.9	1.91	0.07
Ratio of combined to free cholesterol	70	Boys	2.67	0.57		
	71	Girls	2.65	0.51		
	141	Both sexes	2.66	0.54	0.03	0.09
Group with Miscellaneous Conditions†						
Free cholesterol	52	Boys	51.5	9.7		
	27	Girls	53.8	9.0		
	79	Both sexes	52.3	9.6	0.73	1.45
Total cholesterol	54	Boys	173.0	31.2		
	26	Girls	194.5	40.2		
	80	Both sexes	182.7	35.4	2.66	0.11
Ratio of combined to free cholesterol	54	Boys	2.54	0.48		
	27	Girls	2.72	0.48		
	81	Both sexes	2.63	0.48	0.035	0.25
All Groups Combined						
Free cholesterol	170	Boys	50.2	9.8		
	155	Girls	51.0	10.9		
	325	Both sexes	50.6	10.3	0.37	....
Total cholesterol	176	Boys	182.4	36.8		
	154	Girls	185.3	39.9		
	330	Both sexes	183.7	38.7	1.85	....
Ratio of combined to free cholesterol	172	Boys	2.68	0.54		
	153	Girls	2.67	0.52		
	325	Both sexes	2.65	0.53	0.02	....

* Two free cholesterol values of 89 and 99 mg. were dropped, as were the two ratios involved. Also, two additional ratios of over 5, which differed from the mean by more than four times the standard deviation, were discarded.

† Two free and one total cholesterol value were discarded because of probable errors in technic. These were 94, 101 and 478, respectively.

with a failing heart, medication and elevation of the white cell count, in addition to variations in the pulse rate, the temperature and the rate of sedimentation of the erythocytes, will be described in a later paper. In comparing the results for the patients with rheumatic fever (table 2) with those for the patients with infection of tonsils and adenoids, a

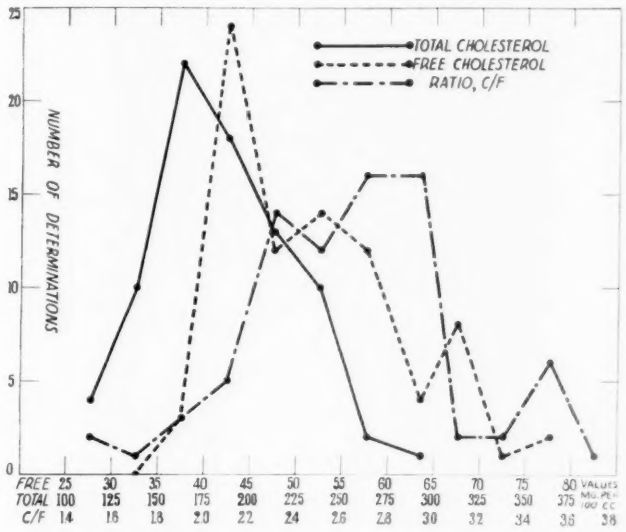

Chart 3.—Curves showing the frequency of values for the free and for the total cholesterol and the ratio of combined to free cholesterol for the group with miscellaneous conditions.

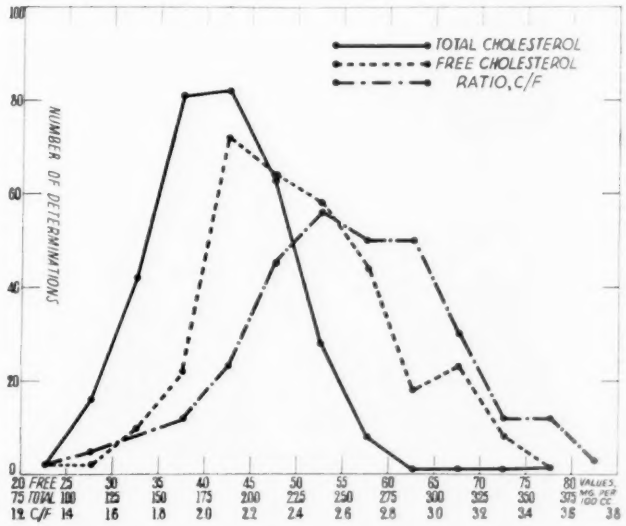

Chart 4.—Curves showing the frequency of values for the free and the total cholesterol and the ratio of combined to free cholesterol for the three groups.

striking similarity is seen, with equally low values for the probable errors of the means. It is interesting to note the smaller range of the standard deviations for this group; the deviations were less than 20 per cent of the respective means, although the complete range of individual values, as may be seen in figure 2, was as extensive as that for the patients with infection of the tonsils and adenoids. There is almost

TABLE 3.—*Values for the Free and the Total Cholesterol and the Ratio of Combined to Free Cholesterol, Arranged by Age Divisions*

	Number of Cases	Sex	Mean Value, Mg. per 100 Cc.	Standard Deviation
		Age Group of from 2 Months to 3 Years		
Free cholesterol	19	Boys	51.1	10.4
	11	Girls	52.5	10.7
	30	Both sexes	51.6	10.5
Total cholesterol	19	Boys	171.4	44.5
	10	Girls	179.2	47.6
	29	Both sexes	174.1	45.3
Ratio of combined to free cholesterol	19	Boys	2.47	0.55
	11	Girls	2.57	0.49
	30	Both sexes	2.52	0.53
		Age Group of 4, 5 and 6 Years		
Free cholesterol	51	Boys	48.9	8.6
	40	Girls	50.0	10.1
	91	Both sexes	49.8	9.9
Total cholesterol	54	Boys	175.7	27.9
	39	Girls	179.9	33.8
	93	Both sexes	177.5	30.4
Ratio of combined to free cholesterol	52	Boys	2.65	0.44
	40	Girls	2.59	0.57
	92	Both sexes	2.63	0.50
		Age Group of 7, 8 and 9 Years		
Free cholesterol	48	Boys	51.1	10.1
	56	Girls	51.4	9.0
	104	Both sexes	51.2	9.5
Total cholesterol	49	Boys	185.8	38.0
	56	Girls	192.7	46.1
	105	Both sexes	189.5	42.2
Ratio of combined to free cholesterol	48	Boys	2.74	0.69
	54	Girls	2.70	0.51
	102	Both sexes	2.73	0.61
		Age Group of 10, 11 and 12 Years		
Free cholesterol	51	Boys	49.9	9.8
	47	Girls	51.1	13.2
	98	Both sexes	50.5	12.4
Total cholesterol	53	Boys	189.1	41.8
	48	Girls	180.9	35.4
	101	Both sexes	185.7	39.2
Ratio of combined to free cholesterol	53	Boys	2.73	0.44
	47	Girls	2.57	0.50
	100	Both sexes	2.65	0.48

no skewing of the curve for free cholesterol values, which indicates a distribution of values that more nearly conforms to the hypothetical distribution curve. Likewise, there were no statistically significant differences between the means for the combined groups (boys and girls) of the patients with rheumatic fever and means for the similar groups of the patients with infection of tonsils and adenoids. This is indicated by the significance value, which should be at least 3 to be of importance (table 2).

The group with miscellaneous conditions consisted of seventy-seven patients with the pathologic conditions previously listed. A total of eighty-one determinations were made. As shown in table 2, the values obtained for this group did not differ significantly from those for the normal group. The standard deviations, again, were less than 20 per cent of the respective means, and the probable errors of the means, as well as the significance value, were likewise small. Figure 3 shows the same marked skewing to the right of the curve for free cholesterol values as was found for the patient with infection of tonsils and adenoids.

A summation of the results of the entire 330 determinations for the three groups studied is presented in table 2. Figure 4 shows the complete range of values. There is a moderate skewing to the right of the curve for free cholesterol.

Since the values for all groups were similar, all the patients studied may be considered as constituting a homogeneous group. On this basis, the patients were divided into four age divisions: (1) those from 2 months to 3 years of age, (2) those 4, 5 and 6 years of age, (3) those 7, 8 and 9 years of age and (4) those 10, 11 and 12 years of age. Table 3 gives the values obtained for these age groups. Although the values for free cholesterol were similar for each division, the total cholesterol values were somewhat lower for younger children than for the older ones. These values are in accord with the generally higher cholesterol values for adults.

COMMENT

If an equable distribution of patients as to age is maintained, it seems apparent that several series of cholesterol determinations on blood serum will give similar mean values, regardless of the pathologic conditions of the patients as grouped in this study. It is undoubtedly justifiable to establish normal values by the use of specimens of blood taken during fasting from patients with involvement of the tonsils and adenoids. The failure of the values for the other groups to deviate widely, the maintenance of similar values for the two sexes within the groups, the trend toward a lower ester cholesterol value at the lowermost age level, the lack of any sort of correlation between free or total cholesterol values and the percentage under or over normal weight—all these point to a deeper meaning for variations in serum cholesterol values in children than merely that they result from changes due to given pathologic conditions. The skewing to the right of the curve for free cholesterol for the patients with involvement of the tonsils and adenoids, and for the miscellaneous group may have significance, although this phenomenon is frequently observed in distribution curves for many types of normal findings. The skewing of any curve to the right indicates a greater variation of findings toward the higher side

of the curve than toward the lower. Since the mode for such a curve (the point of the largest number of values) must be toward the lower range of values for the curve, it follows that a larger percentage of values will fall on the higher side of the mode than on the lower. The fact that the tendency for a larger portion of values to fall within the higher range of the distribution curve occurs only for the free cholesterol fraction and not for the total cholesterol brings to bear certain recent investigations on cholesterol. Bloor, Okey and Corner [21] and Boyd [22] found that an increase in activity in a tissue is definitely characterized by a rise in the free cholesterol content as well as a rise in the phospholipid content and a fall in the ester cholesterol content. The higher metabolic gradient for children has long been an accepted fact, and it may be that the tendency to a greater frequency of values in the higher levels of the distribution curve is an expression of this truth. Perhaps studies of metabolism done simultaneously with analyses of the serum lipids in children will shed more light on this matter.

The lack of variation in values according to sex is perhaps to be expected for patients who are below the age of puberty. It is interesting, however, that this lack of differentiation holds true even for the immediate prepuberty age group, children of 10, 11 and 12 years, in whom premenstrual changes in the serum cholesterol concentration should be manifest if they exist.

SUMMARY

The results of a series of determinations of the cholesterol content of the blood serum have been presented; 330 analyses were made for 250 patients ranging in age from 2 months to 12 years and about equally divided between the sexes. The patients were divided into three groups: (1) those with involvement of the tonsils and adenoids, (2) those with rheumatic fever and (3) those with one of a miscellaneous group of acute and chronic conditions. The values for the first group were 183.4 mg. per hundred cubic centimeters $\pm$ 46.8 and 49.9 mg. $\pm$ 12.1 for the total and the free cholesterol, respectively, and 2.67 $\pm$ 0.55 for the ratio of combined to free cholesterol. These may be regarded as normal values. For the second and third groups the mean values were similar to the normal values. Distribution curves for free cholesterol for the first and third groups show a marked skewing to the right, while the curve for free cholesterol for the second

21. Bloor, W. R.; Okey, R., and Corner, G. W.: The Relation of Lipids to Physiological Activity, J. Biol. Chem. **86**:291 (Feb.) 1930.

22. Boyd, E. M.: The Post-Operative Activity of White Blood Cells as Measured by Their Lipid Content, Canad. M. A. J. **31**:626 (Dec.) 1934; The Lipid Content of the White Blood Cells of Women During Pregnancy, Lactation and Puerperium, Surg., Gynec. & Obst. **59**:744 (Nov.) 1934.

group exhibits no such aberration. No significant differences according to sex were found in the various subgroups, which were made up on the basis of either age or pathologic condition. There is a tendency toward a lower ester cholesterol value for patients up to 6 years.

Drs. E. G. Miller Jr., W. M. Sperry and R. Schoenheimer, of the Department of Biological Chemistry, Columbia University, and Dr. A. A. Weech, of the Department of Diseases of Children, Columbia University, gave valuable assistance in this work.

EFFECT OF MOCCASIN VENOM ON URINARY CHANGES IN SCARLET FEVER

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AND

SAMUEL M. PECK, M.D.

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PROCEDURE

Forty-two boys, aged from 5 to 14 years, with scarlet fever were selected at the Willard Parker Hospital for these observations. (Girls were not included because of the difficulty of obtaining uncontaminated specimens of urine.) Twenty-two were treated with injections of moccasin venom (1:3,000) subcutaneously, and twenty others were used as controls, the division being arbitrary on admission of the patients. Patients who had received scarlet fever antitoxin were excluded.

The administration of moccasin venom was begun on admission, usually on the second or third day of illness; the plan of treatment was to give courses of eight, twelve or sixteen injections. The dose for the first injection was 0.5 cc.; if there was no untoward reaction, 1 cc. was given daily thereafter until half the course was completed; the remainder was administered in doses of 1 cc. every other day. In most of the cases there was a local reaction of sensitivity after the seventh dose, regardless of the frequency with which the venom had been administered. The reaction consisted of an area of redness, induration and heat, varying in diameter from 3 to 15 cm. With these patients the original plan of treatment was abandoned in favor of desensitization, which was accomplished by decreasing the dose to 0.05 cc. and then increasing it gradually, according to the intensity of the previous reaction, as advocated by Peck.[1] No general protein reaction to the venom was noted.

The stay of the patients in the hospital varied between a minimum of thirty days and a maximum of forty-three days, if associated complications were present. Daily Addis counts of the urinary sediment were made for both the patients who were given injections and the controls. In both groups in some of the patients complications of scarlet fever developed such as cervical or mesenteric adenitis and otitis media. The number of children who exhibited complications was approximately the same in the two groups, that is, six of the twenty patients used as controls and nine of the twenty-two patients who were treated with venom. The object of this experiment and the theoretical considerations which led up to the work are made clear in the comment which follows.

From the Willard Parker Hospital, the Mount Sinai Hospital and the Department of Diseases of Children, College of Physicians and Surgeons, Columbia University.

1. Peck, S. M.: Sensitization and Desensitization in Man with Snake Venom (Ancistrodon Piscivorus), Arch. Dermat. & Syph. **27**:312 (Feb.) 1933.

COMMENT

In 1929 Shwartzman [2] found that if a rabbit is given an intradermal injection of undiluted "agar washings filtrates" of organisms, such as typhoid or colon bacilli or meningococci, and that if the same filtrate is injected intravenously twenty-four hours later, a local hemorrhagic necrosis occurs at the site of the initial injection. Not all rabbits show this phenomenon; the number of animals that show a negative reaction depends to a certain extent on the concentration, amount and type of bacterial filtrate.

Peck and Sobotka [3] tested the skin of rabbits with different types of venom capable of producing a primary purpuric reaction, in order to determine whether any relation could be established between the intensity of the purpura and the susceptibility of the animal to the Shwartzman phenomenon. It was noted that those animals in which intense purpura develops after intradermal injection of diluted snake venom are more likely to exhibit a Shwartzman phenomenon than are those which show a slight reaction. A significant observation was the fact that if from fourteen days to one month elapsed between the injection of 0.1 cc. of the dilution of venom into the rabbits and the attempt to elicit the Shwartzman phenomenon, a large number of rabbits proved to be refractory; in other words, venom is capable of inhibiting the Shwartzman phenomenon. Of the various types of venom used in the experiments, that from the moccasin was most potent in rendering animals refractory.

The Shwartzman phenomenon probably depends on an increase in vulnerability of the capillaries at the site of the primary injection. The refractory state to the Shwartzman phenomenon produced by venom could conceivably result either from some circulating substance or from a general effect of the venom on the walls of the capillaries, which makes them resistant to hemorrhage. The evidence against a humoral mechanism is the fact that no antibody or other substance which inhibits the Shwartzman reaction has been demonstrated. The refractory condition cannot be transferred passively with serum from refractory rabbits. It has been suggested that the action may be similar to that of a foreign protein, but one of us (Peck [4]) showed that the factor in moccasin venom which induces the refractory state can be

2. Shwartzman, Gregory: Studies on Bacillus Typhosus Toxic Substances: I. Phenomenon of Local Skin Reactivity to B. Typhosus Culture Filtrate, J. Exper. Med. **48**:247 (Dec.) 1928.

3. Peck, S. M., and Sobotka, H.: Production of a Refractory State as Concerns the Shwartzman Phenomenon by Injections of Venom of the Moccasin Snake (Ancistrodon Piscivorus), J. Exper. Med. **54**:407 (Sept.) 1931.

4. Peck, S. M.: A Refractory State as Concerns the Shwartzman Phenomenon: II. Inhibition of Refractivity Producing Factors in Moccasin Venom by Antivenom and Normal Horse Serum, J. Immunol. **27**:1 (July) 1934.

neutralized or inhibited by antivenin in most cases and by normal horse serum in some cases. The inhibitory effect of venom cannot be due to foreign protein, for the addition of more protein actually prevents the effect of the venom. Antivenin alone in large amounts has no effect on the course of the Shwartzman phenomenon.[4]

There is evidence to indicate that the refractory state induced in animals that were previously given venom is due to changes in the walls of the capillaries. In studying a number of patients with pathologic conditions in which bleeding is a common symptom, one of us (Peck) and collaborators [5] noted that injections of venom arrested hemorrhage in those disorders which were not associated with changes in the blood, namely, functional uterine bleeding, recurrent nasal hemorrhages due to multiple telangiectases, symptomatic purpura and Osler's disease (hereditary telangiectases). In the last condition it was found that the dilated vessels in the mucosa gradually decreased in size and disappeared as the bleeding was controlled. In hemorrhagic diseases associated with definite changes in the blood, the results were not satisfactory. In hemophilia, in which the changes are limited to the clotting mechanism, the venom had no effect. In purpura haemorrhagica, in which there may be changes in the capillary walls as well as in the blood, bleeding was often controlled even though the low numbers of platelets persisted. It was also found that an injection of venom into a patient with purpura haemorrhagica produced a large ecchymosis at the site of injection. With the gradual control of bleeding, the ecchymotic reaction to the venom slowly disappeared. In patients with purpura haemorrhagica in whom the condition was not controlled by the venom, the ecchymotic reaction to the venom usually persisted.

In 1933, one of us (Lyttle [6]) applied the technic of Addis for the quantitative mensuration of protein, casts and blood cells in the urine in fourteen cases of scarlet fever. It was noted that in all cases there was a moderate transient explosive increase in the excretion of protein and formed elements for from eight to forty-five days after the onset of scarlet fever. Using the routine methods of analysis of urine, other workers observed the same changes in urine of patients convalescing from scarlet fever. Later studies were carried out on other groups of patients with scarlet fever and with other types of infection due to hemolytic streptococci. It was observed that subclinical nephritis

5. Peck, S. M.: Attempts at Treatment of Hemorrhagic Diathesis by Injection of Snake Venom, Proc. Soc. Exper. Biol. & Med. **29**:579 (Feb.) 1932. Peck, S. M., and Goldberger, M. A.: The Treatment of Uterine Bleeding with Snake Venom, Am. J. Obst. & Gynec. **25**:887 (June) 1933. Peck, S. M., and Rosenthal, N.: Effect of Moccasin Snake Venom (Ancistrodon Piscivorus) in Hemorrhagic Conditions, J. A. M. A. **104**:1066 (March 30) 1935.

6. Lyttle, J. D.: The Addis Sediment Count in Scarlet Fever, J. Clin. Investigation **12**:95 (Jan.) 1933.

occurred consistently after infection with hemolytic streptococci. While no extrarenal signs or symptoms were observed at the time of the urinary abnormalities, it is reasonable to assume that the reaction was due to the same mechanism that sets up a clinical attack of glomerulonephritis, the difference being one of degree.

There is much clinical as well as pathologic evidence to indicate that glomerulonephritis is caused by generalized damage to capillaries. The Shwartzman reaction, like the lesions in glomerulonephritis, is essentially a vascular phenomenon, probably involving the capillaries. The fact that the Shwartzman phenomenon can be inhibited by snake venom led Baehr to state the belief that moccasin venom injected early in the course of scarlet fever might render the renal capillaries resistant to the damage known to follow streptococcic infection and thereby pre-

Summary of Results

	Patients Used as Controls			Patients Treated with Moccasin Venom		
	Frequency	Number of Cases	Percentage	Frequency	Number of Cases	Percentage
Protein above 0.02%	4	1	5	4	4	18
Casts, millions per 12 hours						
0.05-0.1	15	6	30	11	6	27
0.1 -1.0	32	6	30	7	3	13
Above 1.0	3	3	15	1	1	4.5
R.B.C., millions per 12 hours						
2.0- 5.0	81	18	90	89	19	86
5.0-10.0	17	6	30	10	5	23
Above 10.0	8	5	25	6	4	18
W.B.C., millions per 12 hours						
2.0-5.0	12	6	30	6	4	18
Above 5.0	5	2	10	1	1	4.5
Total number of counts of urinary sediment		399			426	
Total number of cases		20			22	

vent the development of mild urinary explosions or of subclinical and perhaps even clinical nephritis.

As Flexner and Noguchi [7] have shown that definite changes in the glomeruli can be produced by snake venom administered in toxic amounts, it seemed important to know whether moccasin venom in therapeutic doses had any adverse effect on the vessels of the kidneys, as indicated by the sensitive Addis count. This question has often arisen in the course of venom therapy. Thus far no damage to the kidneys has been observed in either animals or human beings treated with venom. If the kidneys of a patient exposed to scarlet fever toxin are not injured by venom, there is little likelihood of damage to the normal renal vascular bed as the result of the administration of the same concentration of venom.

7. Flexner, S., and Noguchi, H.: On the Plurality of Cytolysins in Snake Venom, J. Path. & Bact. **10**:111, 1905.

RESULTS

The results are summarized in the table. Those for eight typical cases are shown in charts I and II. We have excluded one case of clinical nephritis (in which no treatment was given), since we were interested only in subclinical nephritis. All children in the control and untreated groups at some time in the period of from eight to forty-

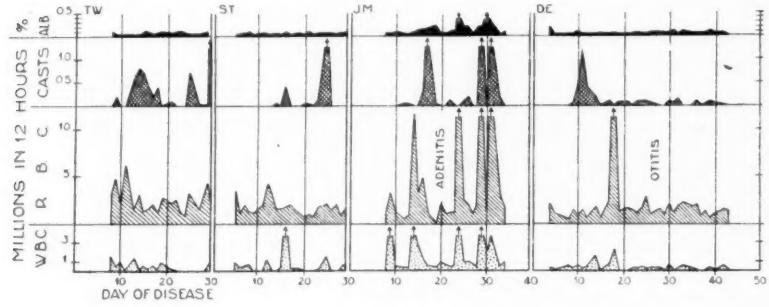

Fig. 1.—Results of quantitative studies of urine of four patients with scarlet fever who were not treated with moccasin venom.

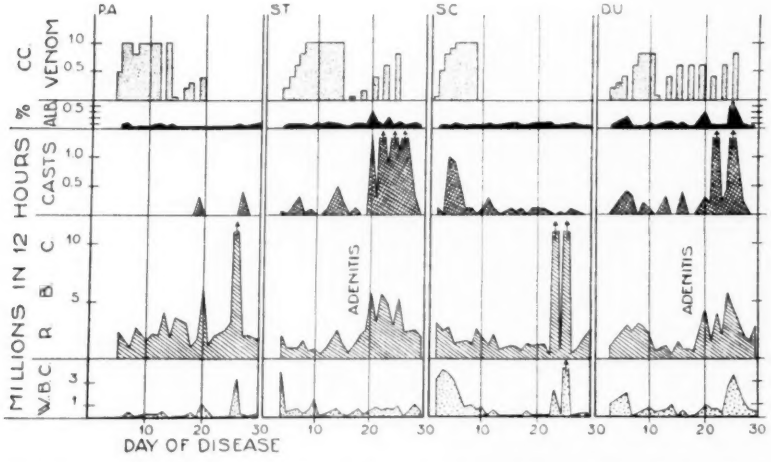

Fig. 2.—Results of quantitative studies of urine of four patients with scarlet fever who were treated with moccasin venom.

three days after the onset of scarlet fever showed the expected increase in the excretion of formed elements. In some cases the changes, though definitely abnormal, were slight; in others they were more decided. We believe that the excretion of casts and red cells is a more delicate indication of renal irritation than is the excretion of protein, of epithelial cells or of leukocytes.

The normal excretion of casts in twelve hours for children in this age group is under 20,000. In the control group the excretion of casts was above 100,000 per twelve hours thirty-five times in nine cases as compared to eight times in four cases in the group of patients treated. These differences cannot be considered significant, because the rate of excretion of casts is variable, especially when uniform conditions are not maintained. For therapeutic reasons it was impossible to restrict the intake of fluids so as to insure constant urinary acidity and concentration.

Normal children usually excrete under 500,000 red cells in the urine in twelve hours. Those in the control group excreted above 5,000,000 in twelve hours twenty-five times in eleven cases as compared to sixteen times in nine cases in the treated group. Excretion of red cells above 10,000,000 in twelve hours occurred eight times in five cases in the control group and six times in four cases in the treated group. Clearly the slight differences cannot be interpreted as significant.

CONCLUSION

Moccasin venom in the dosage used: (1) did not prevent the occurrence of moderate urinary changes (subclinical nephritis) in twenty-two cases of scarlet fever and (2) gave no evidence of damage to renal capillaries.

SECOND ATTACKS OF POLIOMYELITIS IN MACACUS RHESUS MONKEYS

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During the past three years seventy-one Macacus rhesus monkeys were given injections of combinations of poliomyelitis virus either into the subserosa or into the small intestine, between clamps placed in a manner previously described.[1] In thirteen of the animals quadriplegia developed, and all but one died. Seven showed merely a fleeting muscular weakness, while each of the remaining fifty-one monkeys had obvious monoparesis or monoplegia, paraparesis or paraplegia or a combination of both. After recovery fifteen of the fifty-one animals had atrophy of some group of muscles, which in most instances was limited to one leg.

A study is in progress of the pathologic changes that occurred in the central nervous systems of the Macacus rhesus monkey after the introduction of poliomyelitis virus by way of the gastro-intestinal tract, and the observations will be given in detail later.[2] In passing, however, it can be said that in the animals that were killed within three or four days after the introduction of virus by this portal of entry, the following conditions were observed: a massive destruction of the anterior horn cells with edema and an increase in the number of neuroglia cells. In addition to the foregoing changes, in those that died later the usual perivascular cuffing and infiltration of round cells were noted.

A 1 per cent suspension in saline solution of the lumbar portions of the cords of twelve of the animals that died was injected intracerebrally into twelve other monkeys. The disease was produced in each of them: eleven became quadriplegic and died, one showed weakness of the upper and paralysis of the lower extremities and lived. In each instance the pathologic changes seen in microscopic sections were typical: perivascular cuffing, lymphocytic infiltration, etc. Eight other animals were given injections intracerebrally of 0.4 cc. of a combination of equal amounts of a 1 per cent suspension of poliomyelitis virus

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1. Toomey, John A.: Spread of Poliomyelitis from the Gastro-Intestinal Tract, Proc. Soc. Exper. Biol. & Med. **31**:680, 1934.

2. Toomey, John A.: Pathologic Reactions in the Cords of Macacus Rhesus Monkeys Following Introduction of the Virus by Way of the Gastro-Intestinal Tract, to be published.

made from the cords of monkeys that died after an injection into the gastro-intestinal tract of virus and human convalescent poliomyelitis serum. There was neutralization, since the disease was not produced, while two controls which were given injections of saline solution and virus suspension, combined in the same percentage, became paralyzed. Thus paresis or paralysis was produced in the experimental animal after the injection of the virus by way of the gastro-intestinal tract. It was likewise demonstrated that the virus could be recovered from the animal that died, because a suspension made from the spinal cords of these monkeys produced the disease when it was injected into other animals. It was obvious that the recovered virus was specific, since it was neutralized by convalescent human serum.

In the animals in which only monoparesis or monoplegia occurred, the paralysis was usually observed in the leg; when quadriplegia occurred, the paralysis started in the legs and later involved the arms.

It has been previously shown that the virus may spread along the nerve fibers [3] of the sympathetic system. Since there is an obvious direct connection between the cord and the intestine by way of the sympathetic nerve fibers,[4] it is logical to assume that in the animal in which the virus was introduced by way of the gastro-intestinal system the virus spread from the intestine to the cord by way of this connection.

Nine of the animals mentioned that had had paresis or paralysis of one or two members after the injection of the virus by way of the gastro-intestinal tract and had recovered, as well as the one animal that survived the quadriplegic condition, were then given injections of homologous virus intracerebrally at various times. In nine of the ten animals quadriplegia developed; the only animal that escaped had had quadriplegia after the previous injection. Although infantile paralysis had certainly been produced when the virus was introduced via the gastro-intestinal route, and although the ten animals selected had had paresis or paraplegia and even fixation atrophy of certain groups of muscles, it was obvious that none of the animals was immunized by the previous injection of virus into the gastro-intestinal tract against a subsequent intracerebral injection of virus. The clinical history of the only animal that recovered showed that after the introduction of the homologous virus by way of the gastro-intestinal tract, paralysis or paresis of the muscles of both the upper and the lower extremities had developed.

It has long been assumed that the immunity which follows the production of the experimental disease in the monkey is permanent, i. e., is

3. Toomey, John A.: Spread of Poliomyelitis Virus Along Nerve Fibers of the Sympathetic System, Proc. Soc. Exper. Biol. & Med. **31**:502, 1934.

4. (*a*) Round Table Discussion on Poliomyelitis, J. Pediat. **7**:277, 1935. (*b*) Toomey, John A.: An Explanation of the Mechanism of Infantile Paralysis Production in the Human Being, Ann. Int. Med. **8**:854, 1935.

of sufficient strength to protect the animal from the effect of subsequent injections of the virus. Yet the animals in which mild paralysis developed after the virus was introduced via the gastro-intestinal tract were not protected against acquiring the disease after subsequent intracerebral injections of homologous virus. May animals that acquire poliomyelitis after an intracerebral injection be susceptible likewise to the effect of a second intracerebral injection of virus, and if so, under what circumstances?

In the past few years, eighteen of over four hundred Macacus rhesus monkeys that acquired experimental poliomyelitis have lived. Some of these animals were first given injections of poliomyelitis virus by way of the gastro-intestinal tract. Eighteen monkeys had been given injections as noted in the protocol. Six animals (468, 453, 470, 477, 92 and 411) that had previously been given injections intracerebrally contracted the disease again after a second intracerebral injection. Six animals (461, 462, 467, 218, 219 and 238) previously given injections intracerebrally did not respond to subsequent intracerebral injections. Two animals (211 and 213) did not respond to an increase in the doses of the material injected intracerebrally after they had once acquired a massive attack of the disease. Monkey 265, which had first received an injection of virus into the sciatic nerve and which had contracted the disease, was not immune to subsequent intracerebral injections. However, after severe quadriplegia developed, it was able to withstand another massive intracerebral injection of virus. Monkeys 273 and 280, which had received their first injection of virus by way of the vagus nerve and which had acquired the disease, contracted it again after the intracerebral injection of virus; however, the second attack was milder, probably demonstrating that some protection had occurred after the first injection. Animal 285 received the first injection via the vagus nerve, contracted the disease and recovered. It survived one subsequent intracerebral injection but succumbed to a third massive dose, given the same way.

The clinical histories of the eight animals that were not definitely disturbed by a second or subsequent intracerebral injection of virus showed that the original clinical attack was massive; quadriplegia occurred at some time or another in six (461, 462, 467, 211, 213 and 218) and a condition nearly that of quadriplegia in the other two (219 and 238). When the monkeys that had quadriplegia survived, there was recovery of most or many of the groups of muscles of the upper extremities, while the legs usually became fixed and functionless. Thus it was easy to determine whether there was a clinical attack of the disease after a subsequent intracerebral injection by studying the muscles of the arms. Of the group that contracted the disease a second

Protocol

Monkey Number	Date of Injection	Amount Injected, Cc.	Concentration of Virus Suspension	Route of injection	Result
468	7/16/35	150.0	1%	Gastro-intestinal	Transient weakness of legs
	8/13/35	0.3	1%	Intracerebral	Paralysis of left foot and left arm
	9/ 3/35	0.2	10%	Intracerebral	No change
	10/ 8/35	2.0	5% purified	Intracerebral	Quadriplegia 10/17/35 and death
453	4/23/35	0.2	2%	Intracerebral	Paresis of both legs; some fixation atrophy of right leg
	10/22/35	2.0	5% purified	Intracerebral	Quadriplegia, 10/30/35
	11/10/35	2.0	10% purified	Intracerebral	No response
470	7/22/35	150.0	1%	Gastro-intestinal	Transient weakness of legs
	8/13/35	0.3	1%	Intracerebral	Furred; paresis of legs; atrophy of muscles of leg
	9/ 3/35	0.2	10% purified	Intracerebral	Quadriplegia, 9/13/35
	11/10/35	2.0	10% purified	Intracerebral	No response
477	5/31/35	0.15	20%	Left facial nerve	Weakness; cannot close left eyelid, 6/5/35
	8/ 8/35	0.2	1%	Intracerebral	Tremor; paresis of legs; recovered
	9/23/35	30.0	5%	Subserosal	Paralysis of both feet and legs, more marked on left; recovered
	11/12/35	2.0	5% purified	Intracerebral	Definite paralysis of left leg and foot; recovered, with atrophy of muscles of left leg
92	3/28/34	0.5	1%	Intracerebral	Paralysis of left leg and foot and right arm; recovered, with atrophy of left leg
	5/16/34	2.0	1%	Intracerebral	Quadriplegia, 5/23/34; recovered use of upper extremities
	2/12/35	2.0	10%	Intracerebral	No response
411	2/12/35	0.25	1%	Intracerebral	Incoordinate; clumsy; paresis of leg; recovered
	6/12/35	0.5	20%	Intracerebral	Quadriplegia, 6/18/35
	8/20/35	2.0	10%	Intracerebral	No response
461	7/ 8/35	0.2	1%	Intracerebral	Quadriplegia, 7/18/35; recovered, with atrophy of both legs
	9/23/35	30.0	5%	Subserosal	Furred; no extension
	11/12/35	2.0	10%	Intracerebral	No response
462	7/13/35	130.0	1%	Gastro-intestinal between clamps	Tremor; paralysis of both lower extremities and left arm; fixation atrophy of both legs; recovered use of left arm
	8/13/35	0.3	1%	Intracerebral	Tremor; clumsy
	9/ 3/35	0.5	5%	Intracerebral	No reaction
	10/ 8/35	2.0	5%	Intracerebral	Tremor
	10/22/35	2.0	10% purified	Intracerebral	No response
467	7/13/35	135.0	1%	Gastro-intestinal between clamps	Furred; no paralysis
	8/13/35	0.3	1%	Intracerebral	Paralysis of all four extremities; recovered some arm movements; developed atrophy of lower right extremity
	9/ 3/35	0.5	5%	Intracerebral	Weak; furred; no further paralysis
	10/ 8/35	2.0	5%	Intracerebral	Tremor; furred
	10/22/35	2.0	10%	Intracerebral	No response
211	4/ 2/34	25.0	1%	Subserosal	Paralysis left foot and leg; paresis of right foot; left hand weak; recovered, with atrophy of left leg
	5/16/34	2.0	1%	Intracerebral	Quadriplegia; recovered, with atrophy of both legs and left hand
	2/ 2/35	1.5	10%	Intracerebral	No response
213	4/ 4/34	25.0	2%	Subserosal	Paresis of left foot and leg, thigh, and right foot; atrophy of left foot and leg
	5/16/34	2.0	1%	Intracerebral	Quadriplegia, 5/20/34
	2/ 2/35	1.5	10%	Intracerebral	Atrophy fixation of both legs and right hand before injection; no response
	3/12/35	2.0	10%	Intracerebral	No response

Intracerebral

Monkey Number	Date of Injection	Amount Injected, Cc.	Concentration of Virus Suspension	Route of Injection	Result
218	4/11/34	0.2	10%	Intracerebral	Paralysis of both lower extremities; paresis of both upper extremities, 4/24/34
	5/16/34	2.0	1%	Intracerebral	Furred; no change
	2/ 2/35	1.5	10%	Intracerebral	Fixation atrophy of both legs before injection; can slide about; no response
219	4/21/34	1.0	10%	Intracerebral	Paralysis of left leg; paresis of both arms; dragged himself in walking; recovered, with fixation atrophy
	2/ 2/35	1.5	10%	Intracerebral	Before injection, left leg was atrophic; nails in pad and left hand atrophic; no response
238	5/28/34	2.0	10%	Intracerebral	Paralysis of muscles of left foot, thigh and hand, and right foot; recovered, with atrophy of right foot
	10/10/34	0.75	1%	Intracerebral	Before injection, moved about on buttocks; both legs fixed and atrophic; tremor; no change
	6/13/35	0.5	10%	Intracerebral	Before injection, atrophy fixation of right foot, leg, thigh and arm, and left leg; moved about by sliding on buttocks; furred; tremor; no other response
	10/11/35	2.0	1%	Intracerebral	No response
265	10/24/34	0.25	2%	Sciatic nerve	Paralysis of left leg and foot, 11/5/34; paresis of right leg and foot; residual weakness of left leg
	12/21/34	0.4	2%	Intracerebral	Quadriplegia, 12/30/34
	2/12/35	2.0	10%	Intracerebral	No response
273	11/ 6/34	0.15	2%	Vagus nerve	Paralysis of both feet and left leg; recovered, with atrophy of left leg
	12/21/34	0.4	20%	Intracerebral	Paresis both feet, most marked on left; ptosis of right eyelid; contraction of right pupil; recovered
	10/11/35	2.0	10%	Intracerebral	No response
289	12/18/34	0.2	1%	Right vagus nerve	Ptosis of right eyelid; pupillary reflex lost, 12/27/34; recovered
	2/12/35	0.25	2%	Intracerebral	Paresis of feet and arms; double ptosis of lids; paralysis of left sternocleidomastoid; recovered
	10/20/35	2.0	10%	Intracerebral	Paraplegia
285	11/28/34	0.2	2%	Right vagus nerve	Paresis of both lower and right upper extremities; recovered
	12/21/34	0.4	2%	Intracerebral	No change
	2/ 2/35	0.2	2%	Sciatic nerve	No change
	3/21/35	1.0	10%	Intracerebral	Quadriplegia, 3/28/35
	8/20/35	2.0	10%	Intracerebral	No response

time, the original attack was milder and was evidenced by paresis of the legs and arms or of the legs or by paralysis of one member or, at the most, of two; in short, a mild attack of disease was found in most instances after the virus was introduced by way of the gastro-intestinal tract.

Control experiments were carried on at the same time to test each batch of virus. The amount injected was always 0.2 cc. of a 1 per cent suspension, and in every instance the control animal contracted poliomyelitis.

The virus used in these experiments was Flexner's mixed virus strain, obtained through Drs. Hudson and Lennette of the University of Chicago, Department of Hygiene and Bacteriology.

COMMENT

About the time the foregoing work was begun, Brodie [5] described seven animals that contracted the disease a second time after he had given them reinjections, with an increase in the number of units of his minimal completely paralyzing dose. Two of the animals, 453 and 468, were slightly affected before the second injection, but monkeys 985, 549, 440, 992 and 168 had unquestionable involvement after the first intracerebral injection; nevertheless, the disease developed a second time when injections of a greater number of minimal completely paralyzing doses were given. It is curious that monkey 992, which had weakness of one arm, and monkey 949, which had a partial paralysis of one arm, complete paralysis of the other and nearly complete paralysis of the leg, succumbed to subsequent injections with an increase in the number of minimal completely paralyzing doses. Neither monkey 985 nor monkey 440 had complete quadriplegia, although all the extremities were involved. Both succumbed to a second larger dose of virus, although monkey 440 seemed to have had some protection, since he suffered only a mild attack.

If an animal is not susceptible to 40 minimal completely paralyzing doses but succumbs to 60, one might conclude that immunity against this disease is relative, although few human beings ever contract the disease a second time.[6] This fact, however, is subject to qualifications based on arithmetical possibilities: Since the number of human beings that actually contract poliomyelitis is relatively small, even in epidemics, it is unlikely that these few persons would be exposed again to the disease. Logically, then, even a few well proved cases of poliomyelitis developing twice in the same patient would indicate that the disease can recur. Three patients who supposedly had recurrent poliomyelitis were admitted to our ward, but in each instance we could point to another infection as the causative factor of the paralysis the second time.

Brodie stated that in the animals that had a mild attack of the disease, with or without transient paralysis, little immunity developed. My experience has been similar. However, the conclusion might be drawn, from the data presented here, that the animals that showed ordinary

5. Brodie, Maurice: The Rôle of Antibody Formation in Monkeys Actively Immunized with Poliomyelitis Virus, J. Immunol. **27**:395, 1934.

6. Quigley, T. B.: Second Attacks of Poliomyelitis: Review of Literature and Report of Case, J. A. M. A. **102**:752 (March 10) 1934.

quadriplegia and recovered, irrespective of the dose of the virus, were probably immune, since they did not contract the disease again even when repeated intracerebral injections were given of doses as high as 2 cc. of a 10 per cent virus suspension. Animal 468 died after it had acquired the disease a second time. The other animals in this group (453, 470, 92 and 411) that had quadriplegia with the second attack of the disease (with the exception of 477) were immune to subsequent injections, even though an injection of 2 cc. of a 10 per cent solution of purified virus was given intracerebrally. Animal 477, although definitely affected, did not have quadriplegia and thus showed some protection.

The initial dose of virus did not determine the type or extent of paralysis, since the paralysis after an injection of 0.2 cc. of a 1 per cent suspension of poliomyelitis virus was as severe as that resulting from an injection of as much as 2 cc. of a 10 per cent solution. An increase in the virus content of the injection accelerated the production of the disease but slightly. Quadriplegia developed between from six to ten days after injection in five animals that were given 0.2 cc. of a 1 per cent solution and also in five others given 2 cc. of a 10 per cent solution of the same virus suspension. Irrespective of the original dose, the animal that had quadriplegia seemed to be protected not only from the usual dose required to produce the disease but from many multiples of that dose.

In one experiment described by Leiner and von Wiesner,[7] a monkey was reinoculated seventeen days after the onset of the original paralysis; ten days later acute symptoms developed and the paralysis became more extensive. This condition may have been a second attack of the disease, but it likewise may have been a relapse. Krauspe [8] observed one monkey that died of severe poliomyelitis after a third reinoculation given four and one-half months after the first. Paul and Trask [9] stated: "It would seem as if the successful reinfection of the monkey by a homologous strain was distinctly uncommon." They reinoculated thirteen animals with virus of a homologous strain, with negative results. They concluded that, "as others have often shown, such instances of reinfection must be uncommon." Yet in my work all the injections

7. Leiner, C., and von Wiesner, R., in Poliomyelitis: A Survey Made Possible by a Grant from the International Committee for the Study of Infantile Paralysis, Baltimore, Williams & Wilkins Company, 1932.

8. Krauspe, in Poliomyelitis: A Survey Made Possible by a Grant from the International Committee for the Study of Infantile Paralysis, Baltimore, Williams & Wilkins Company, 1932.

9. Paul, J. R., and Trask, J. D.: Comparative Study of Recently Isolated Human Strains and Passage Strain of Poliomyelitis Virus, J. Exper. Med. **58**: 513, 1933.

were of suspensions of homologous virus in saline solution. Paul and Trask's lack of success may be due to the fact that they employed the same dose and percentage of virus for both the original and the subsequent injections. When they used a heterologous strain of virus, they were able to reinfect the animals easily, as were Burnet and MacNamara,[10] whose work they had repeated.

It may be that virus differs only quantitatively and not qualitatively. The evidence that there are qualitative differences is based on the generally accepted belief that an animal is not reinfected with a homologous strain of virus but that it may be reinfected with a heterologous strain. This report casts doubt on the validity of the assumption that reinoculation of homologous virus cannot reinfect monkeys.

One wonders if a monkey that has recovered from massive paralysis (quadriplegia) produced by one strain of virus could acquire the disease again by another strain. If such an animal was immune, qualitative differences would have to be measured by some other means.

CONCLUSIONS

Animals that received injections of virus either by way of the gastrointestinal tract or intracerebrally and that had paresis or limited palsies as a result, contracted the disease again when subsequently given injections of homologous virus intracerebrally. Animals that had severe quadriplegia after the introduction of the first or of any subsequent injection of the virus seemed to be protected from the effects of doses ordinarily used in experimental work.

10. Burnet, F. M., and MacNamara, J.: Immunological Differences Between Strains of Poliomyelitic Virus, Brit. J. Exper. Path. **12**:57, 1931.

RESPIRATORY METABOLISM IN INFANCY AND IN CHILDHOOD

XVIII. THE RESPIRATORY EXCHANGE IN PREMATURE INFANTS—BASAL METABOLISM

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The nature of the defect in the regulation of body temperature by premature infants is not precisely defined. The facility with which subnormal body temperatures develop in these subjects implies the existence of a tendency for the loss of heat to exceed the production. Whether this imbalance is ascribable to an abnormally low production, an excessive loss or a combination of the two has not heretofore been systematically studied.

The purpose of our investigation was to collect data which might clarify the nature of the underlying defect. This paper is concerned with the heat production of premature infants. It reports sixty-four observations, in two groups, of the basal metabolism of twenty-two infants: in the first group, twenty-six observations on twelve infants under environmental conditions not rigidly controlled, and in the second group, thirty-eight observations on ten infants in an air-conditioned suite.

The literature contains three comprehensive studies of the basal metabolism of premature infants [1] and several scattered reports.[2] In general, the authors concluded that these subjects have a low basal

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1. (*a*) Marsh, M. E., and Murlin, J. R.: Energy Metabolism of Premature and Undersized Infants, Am. J. Dis. Child. **30**:310 (Sept.) 1925. (*b*) Talbot, F. B.; Sisson, W. R.; Moriarty, M. E., and Dalrymple, A. J.: The Basal Metabolism of Prematurity, ibid. **26**:29 (July) 1923. (*c*) Schadow, H.: Der Betriebstoffwechsel und Kalorienbedarf frühgeborener Säuglinge, Jahrb. f. Kinderh. **136**:1, 1932.

2. (*a*) Rubner, M., and Langstein, L.: Energie- und Stoffwechsel zweier frühgeborener Säuglinge, Arch. f. Physiol. **39**:39, 1915. (*b*) Schlossman, A., and Murschauser, H.: Gasstoffwechseluntersuchungen bei Neugeborenen und Frühgeborenen, Ztschr. f. Kinderh. **54**:301, 1933. (*c*) Essig, B.: Ueber das Verhalten des Grundumsatzes bei untergewichtigen Säuglingen, Monatschr. f. Kinderh. **53**: 343, 1932. (*d*) Mordhorst, H.: Ueber die chemische Wärmeregulation frühgeborener Säuglinge, ibid. **55**:174, 1932.

metabolism. Their results suggested to us the desirability of employing calorigenic endocrine products in an effort to augment this reported low rate of heat production. It became apparent, however, from a scrutiny of the published reports and our initial group of observations, made under environmental conditions and with a respiratory chamber comparable to those of the earlier studies, that refinements of technic were necessary for a proper appraisal of the contemplated endocrine therapy. The minimal amounts of oxygen consumed and carbon dioxide eliminated by the infants (from 1 to 2 Gm. per hour) suggested the use of a small chamber in an air-conditioned suite, which would obviate the relatively large technical errors induced by comparatively minor environmental fluctuations.

APPARATUS AND METHODS

First Series.—The first group, twenty-six observations, was made with the closed circuit type of apparatus described in earlier papers of this series.[3] It consisted of a Benedict universal respiration table attached to an infant's chamber of 120 liters, comparable in size to that used by previous workers.[1] The balance for weighing the absorption bottles had a capacity of 10 Kg. and a sensitivity of 20 mg. The calorimeter room was equipped with a thermostat, which prevented wide fluctuations in environmental temperature. Evaporation of moisture by an electric fan from a cloth placed on the respiration chamber helped to control the temperature during measurements. The relative humidity of the chamber was regulated by the ventilating system of the apparatus.

The average temperature for individual observations, from forty-five to one hundred and eighty minutes long, in the first series ranged from 24.6 (observation 191) to 28.5 C. (observation 220), the variations for individual periods being from 0.03 to 0.48 C. except in three observations (181, 184 and 197; table 3).

Second Series.—The second series, thirty-eight observations, was made in the air-conditioned suite of the metabolism unit of the Children's Clinic at the New York Hospital. The calorimeter room accommodated the respiration chamber and accessory equipment without hampering the movements of three observers during experiments. The air-conditioning apparatus changed the air of the room completely every four minutes, limiting the fluctuations of the temperature and relative humidity to 0.2 C. and 5 per cent, respectively. The temperature in the chamber was automatically controlled by the circulation of air in the room. When the temperature of the latter was initially set at 25 C., the temperature of the respiration chamber rose to approximately 28 C. during the preliminary period and was stable for the remainder of the observation. The average temperature in all except

3. (*a*) Levine, S. Z., and Wilson, J. R.: The Respiratory Metabolism in Infancy and in Childhood: I. Basal Metabolism in Children, Am. J. Dis. Child. **31**:323 (March) 1926. (*b*) Wilson, J. R.; Levine, S. Z., and Rivkin, H.: The Respiratory Metabolism in Infancy and in Childhood: II. Ketosis and the Respiratory Exchange in Children, ibid. **31**:335 (March) 1926. (*c*) Levine, S. Z.; Wilson, J. R.; Berliner, F., and Rivkin, H.: The Respiratory Metabolism in Infancy and in Childhood: VI. The Specific Dynamic Action of Food in Normal Infants, ibid. **33**:722 (May) 1927.

three observations of this series was between 27 and 29 C., the variations for the individual periods of single observations being from 0.01 to 0.34 C. except in one instance (P2; table 3).

The ventilating system of the respiration apparatus maintained the relative humidity of the chamber at between 35 and 46 per cent in all except six observations (table 3). The variations in the average relative humidity of the individual periods were from 1 to 6 per cent except in two observations (P6, P10). Readings in the chamber were made with a hair hygrometer, which was calibrated daily with a sling psychrometer.

Prior to the second series a number of modifications of the apparatus were made to increase the precision of the measurements. A small chamber, with a volume of 21 liters, was constructed of copper, tin lined, to reduce dead air space to a minimum. It measured 61 by 28 by 12 cm. and had a cut-out in the bottom to hold receptacles for the collection of urine and stools under oil. The cover contained two windows, one at the head, which permitted constant observation of the infant's face, his behavior and any abnormal symptoms, such as cyanosis, peculiar respiration or regurgitation of food, and the other at the foot, which allowed the passage of urine and stools to be timed.

The calorimeter bed consisted of a narrow frame of wood through the sides of which a fish-net cord was woven, the whole being shellacked. The net stretched partially across the lower half of the bed, leaving a central gap for the collection of urine and stools. A narrow pad encased in rubber served as a mattress.

EXPERIMENTAL PROCEDURE

The procedure was identical in the two series except as noted in the following paragraphs. The infants were taken to the metabolism unit from an ordinary air-conditioned nursery for premature infants,[4] where they had been kept in small open cribs in an environment of 77 F. and 65 per cent relative humidity.[5] They were dressed in standard clothes, consisting in the first series of their usual warm wrappings and in the second of a light flannel wrapper or cotton gown, a light cotton shirt, stockings, a bib and a specimen belt. In eight observations the wrapper was omitted (P11 to P15, inclusive, P18, P24 and P26); in one a woolen blanket was used (P34), and in one both the shirt and the wrapper were omitted (P8). These alterations of clothing had no observable effect on the basal metabolic rate.

The standard clothes assured comfort at the temperature at which the observations were made and resulted in only slight changes in the body (rectal) temperature of the infants. This temperature averaged between 36.2 and 37.3 C. (97.16 and 99.14 F.) in all except five instances (observations 184, 202, 204, 219 and P34; table 3), usually dropping slightly during observations. The average decline for the first and the second series was, respectively, 0.4 and 0.3 C. (.72 and .54 F.) with a maximum change of 1 or 0.8 C. (1.8 or 1.4 F) in all except two observations (202, 204; table 3). In these observations the temperature fell 2.2 and 1.4 C. (3.96 and 2.52 F.), respectively.

4. Four infants (R. C., L. C., E. H. and B.; table 3) were taken from unconditioned rooms, in which they had been kept in open cribs.

5. Blackfan, K. D., and Yaglou, C. P.: The Premature Infant: A Study of the Effects of Atmospheric Conditions on Growth and Development, Am. J. Dis. Child. **46**:1175 (Nov., pt. 2) 1933.

According to our usual custom, a small measured meal was given prior to each observation to assure rest, thus permitting a comparison with figures obtained under similar conditions for full term infants.[6] This meal always consisted of breast milk and averaged approximately 13 calories per kilogram of body weight. The infant's daily diet during the period of observation comprised eight feedings of breast milk except in nine instances (observations 200, P7 to P10, inclusive, P18, P19, P26 and P41), in which a formula of evaporated milk was substituted.

After the meal the infant was placed on the bed in the respiratory chamber, and measurements were begun at the end of a preliminary period of from one-half to one hour, during which equilibrium in temperature and humidity was established. In the first series no attempt was made to collect urine; in the second series urine was collected with the aid of small specimen tubes, the cans for stools and urine fitting in the cut-out at the bottom of the chamber.

The sole duty of one of the three observers while calorimetric measurements were being made was to observe and record the activity of the infant from minute to minute by direct inspection through the windows in the cover. Ninety-eight observations were made, but only sixty-four were accepted as basal, because of the infant's activity in the remainder. Only those observations are reported in which the subject was quiet throughout except for occasional movements of adjustment or in which activity was limited to mild restlessness for relatively small fractions of the total period (table 3). Six observations were included in which the infant cried for from one to three minutes, or during from 0.5 to 5.5 per cent of the total observation. According to Murlin,[7] such intervals, even of lusty crying, may have produced a maximum augmentation of the basal metabolic rate of 5.5 per cent in one observation (P30).

CALCULATION OF RESULTS

The heat production was calculated in the customary manner, with the aid of the modified Zuntz-Schumberg tables,[8] from the rate of oxygen consumption, the amount of nitrogen excreted in the urine during the calorimetric periods, of from two to three hours, and the nonprotein respiratory quotient. It was calculated from the amount of carbon dioxide eliminated only when the determination of the oxygen consumption was unsatisfactory, owing either to marked fluctuations in

6. (*a*) Marine, D.; Lowe, B., and Cipra, A.: Possible Influence of Suprarenal Involution in New-Born Infants on Heat Production, J. Metabolic Research **2**:329, 1922. (*b*) Murlin, J. R.; Conklin, R., and Marsh, M. E.: Energy Metabolism of Normal New-Born Babies, Am. J. Dis. Child. **29**:1 (Jan.) 1925. (*c*) Murlin, J. R.: Physiology of Metabolism in Infancy and Childhood, in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923, vol. 1. (*d*) Benedict, F. G., and Talbot, F. B.: Physiology of New-Born Infant, Publication 233, Carnegie Institution of Washington, 1915; Metabolism and Growth from Birth to Puberty, Publication 302, Carnegie Institution of Washington, 1921. (*e*) Levine and others.[3e] (*f*) Levine, S. Z., and Marples, E.: Respiratory Metabolism in Infancy and in Childhood: XII. A Biometric Study of Basal Metabolism in Normal Infants, Am. J. Dis. Child. **41**:1332 (June) 1931.

7. Marsh and Murlin.[1a] Murlin and others.[6b]

8. Zuntz, N., and Schumberg, W. A. E. F.: Studien zu einer Physiologie des Marsches, Berlin, A. Hirschwald, 1901, p. 361. Lusk, G.: Analysis of the Oxidation of Mixtures of Carbohydrate and Fat, J. Biol. Chem. **59**:411, 1924.

TABLE 1.—*Alcohol Checks for Experimental Year (1934-1935)*

Date	Minutes	Alcohol, Gm.	Water			Carbon Dioxide			Oxygen			Respiratory Quotient (Theoretical, 0.667)		Calories, Theoretical
			Theoretical, Gm.	Found, Gm.	Percentage of Error	Theoretical, Gm.	Found, Gm.	Percentage of Error	Theoretical, Gm.	Found, Gm.	Percentage of Error	Found, Gm.	Percentage of Error	
June 23	61	.....	.....	1.167	.....	.....	1.445	.....	.....	1.580	.....	0.665	.....	....
Average per hour		.....	.....	1.148	.....	.....	1.421	.....	.....	1.554	.....	0.665	−0.002	....
June 24	45	.....	.....	0.985	.....	.....	1.314	.....	.....	1.440	.....	0.664	.....	....
	45	.....	.....	0.859	.....	.....	1.141	.....	.....	1.248	.....	0.665	.....	....
Average per hour		0.871	1.139	1.229	+7.9	1.663	1.637	−1.6	1.815	1.792	−1.3	0.664	−0.003	6.16
July 20	60	.....	.....	1.535	.....	.....	1.879	.....	.....	2.088	.....	0.655	.....	....
	45	.....	.....	0.996	.....	.....	1.268	.....	.....	1.344	.....	0.686	.....	....
Average per hour		1.001	1.309	1.446	+10.5	1.912	1.798	−5.9	2.086	1.961	−6.0	0.667	±0.000	7.09
Sept. 28	65	.....	.....	1.801	.....	.....	2.168	.....	.....	.....*	.....	.....	.....	....
	49	.....	.....	1.269	.....	.....	1.547	.....	.....	.....	.....	.....	.....	....
Average per hour		1.066	1.394	1.616	+15.9	2.036	1.955	−4.0	2.221	2.139	−3.7	0.665	−0.002	7.54
Oct. 5	54	.....	.....	1.370	.....	.....	1.591	.....	.....	1.785	.....	0.648	.....	....
	62	.....	.....	1.607	.....	.....	1.954	.....	.....	2.103	.....	0.676	.....	....
Average per hour		0.908	1.186	1.418	+19.5	1.735	1.688	−2.7	1.893	1.851	−2.2	0.663	−0.004	6.43
Oct. 29	70	.....	.....	1.285	.....	.....	1.647	.....	.....	1.771	.....	0.676	.....	....
Average per hour		0.751	0.982	1.101	+12.2	1.436	1.412	−1.7	1.566	1.518	−3.1	0.676	+0.009	5.32
Oct. 30	45	.....	.....	0.883	.....	.....	1.180	.....	.....	1.299	.....	0.661	.....	....
	57	.....	.....	1.090	.....	.....	1.461	.....	.....	1.557	.....	0.682	.....	....
Average per hour		0.851	1.112	1.161	+4.4	1.626	1.554	−4.4	1.774	1.680	−5.3	0.673	+0.006	6.02
Nov. 12	59	.....	.....	1.092	.....	.....	1.360	.....	.....	1.466	.....	0.675	.....	....
Average per hour		0.750	0.980	1.111	+13.3	1.434	1.383	−3.6	1.564	1.491	−4.7	0.675	+0.008	5.31
Nov. 15	52	.....	.....	1.120	.....	.....	1.462	.....	.....	1.589	.....	0.669	.....	....
	49	.....	.....	0.906	.....	.....	1.147	.....	.....	1.277	.....	0.653	.....	....
Average per hour		0.774	1.012	1.136	+12.2	1.479	1.463	−1.1	1.614	1.607	−0.4	0.662	−0.005	5.48
Nov. 29	37	.....	.....	1.180	.....	.....	1.588	.....	.....	1.730	.....	0.668	.....	....
	45	.....	.....	1.333	.....	.....	1.843	.....	.....	2.022	.....	0.663	.....	....
Average per hour		1.326	1.732	1.839	+6.2	2.533	2.510	−0.9	2.763	2.745	−0.7	0.665	−0.002	9.39

Dec. 20	31	.....	.....	1.014	.....	.....	1.333	.....	.....	1.472	.....	0.659	.....	....
	29	.....	.....	1.012	.....	.....	1.393	.....	.....	1.586	.....	0.639	.....	....
Average per hour		1.417	1.852	2.026	+9.4	2.708	2.726	+0.7	2.955	3.058	+3.5	0.648	—0.019†	10.03
Dec. 21	52	.....	.....	1.123	.....	.....	1.507	.....	.....	1.628	.....	0.673	.....	....
	46	.....	.....	1.116	.....	.....	1.505	.....	.....	1.649	.....	0.664	.....	....
Average per hour		1.096	1.432	1.527	+6.6	2.094	2.054	—1.9	2 285	2.234	—2.2	0.668	+0.001	7.76
Jan. 15	51	.....	.....	1.079	.....	.....	1.322	.....	.....	1.488	.....	0.646	.....	....
	55	.....	.....	1.431	.....	.....	1.989	.....	.....	2.097	.....	0.690	.....	....
Average per hour		0.911	1.190	1.298	+9.1	1.740	1.713	—1.6	1.899	1.854	—2.4	0.672	+0.005	6.45
Feb. 5	46	.....	.....	1.087	.....	.....	1.387	.....	.....	1.514	.....	0.666	.....	....
Average per hour		0.962	1.258	1.418	+12.7	1.839	1.809	—1.6	2.007	1.975	—1.6	0.666	—0.001	6.81
Feb. 20	45	.....	.....	1.236	.....	.....	1.652	.....	.....	1.812	.....	0.663	.....	....
	68	.....	.....	1.783	.....	.....	2.447	.....	.....	2.725	.....	0.653	.....	....
Average per hour		1.168	1.526	1.603	+5.0	2.231	2.176	—2.5	2.434	2.409	—1.0	0.657	—0.010	8.27
Feb. 27	46	.....	.....	0.966	.....	.....	1.192	.....	.....	1.353	.....	0.641	.....	....
	48	.....	.....	0.945	.....	.....	1.220	.....	.....	1.315	.....	0.675	.....	....
	46	.....	.....	0.842	.....	.....	1.105	.....	.....	1.183	.....	0.679	.....	....
Average per hour		0.811	1.060	1.180	+11.3	1.550	1.507	—2.8	1.691	1.650	—2.4	0.664	—0.003	5.74
April 9	46	.....	.....	1.347	.....	.....	1.672	.....	.....	1.800	.....	0.676	.....	....
	53	.....	.....	1.374	.....	.....	1.779	.....	.....	1.984	.....	0.652	.....	....
	35	.....	.....	0.781	.....	.....	1.028	.....	.....	1.186	.....	0.630	.....	....
Average per hour		1.057	1.381	1.561	+13.1	2.019	2.006	—0.7	2.202	2.225	+1.0	0.655	—0.012†	7.48
April 15	65	.....	.....	1.710	.....	.....	2.275	.....	.....	2.564	.....	0.645	.....	....
	45	.....	.....	1.104	.....	.....	1.433	.....	.....	1.523	.....	0.684	.....	....
Average per hour		1.068	1.395	1.535	+10.0	2.041	2.023	—0.9	2.227	2.229	+0.1	0.660	—0.007	7.56
April 16	45	.....	.....	1.221	.....	.....	1.680	.....	.....	1.819	.....	0.672	.....	....
	50	.....	.....	1.195	.....	.....	1.588	.....	.....	1.726	.....	0.669	.....	....
Average per hour		1.098	1.435	1.526	+6.3	2.098	2.064	—1.6	2.289	2.239	—2.2	0.670	+0.003	7.77
May 17	46	.....	.....	0.793	.....	.....	0.959	.....	.....	1.005	.....	0.694	.....	....
	47	.....	.....	0.783	.....	.....	0.932	.....	.....	1.316	.....	0.651	.....	....
Average per hour		0.666	0.870	1.011	+16.2	1.272	1.213	—4.6	1.388	1.314	—5.3	0.672	+0.005	4.71
Total average		0.976	1.276	1.395	+9.3	1.866	1.806	—3.2	2.035	1.976	—2.9	0.665	—0.002	6.91

* Oxygen was not determined for individual periods because of a technical error.
† Marked barometric changes occurred during this observation.

barometric pressure or to movements of the infant during the withdrawal of samples of residual air at the end of the periods.[9]

In calculating the calories in the first series of observations, in which urine was not collected, it was assumed that 15 per cent were derived from protein. The error introduced by this method of calculation is trivial.

In the second series, the protein catabolism was estimated from the amount of nitrogen in the calorimeter specimen.[10] When the latter was expanded in terms of twenty-four hours, it approximated the total daily excretion of nitrogen actually determined for four infants.

ALCOHOL CHECKS

The details of the alcohol checks for the experimental year 1934-1935 (second series) are presented in table 1.

The alcohol lamp was regulated to burn at a rate comparable to the rate of heat production of the infants. The number of calories per hour dissipated by the alcohol flame averaged 6.91, varying from 4.71 to 10, as compared with a range from approximately 3 to 8 calories per hour for the infants. The average respiratory quotient for the series of twenty checks was 0.665, as compared with the theoretical quotient of 0.667. The maximum deviation for an individual observation was less than $\pm$ 0.01 except in two instances (12/20/34 and 4/9/35, table 1). The average error in the value for oxygen consumption from which the rate of heat production was calculated was —2.9 per cent, the maximum being —6 per cent (7/20/34).

The respiratory quotients for the nineteen alcohol checks made during the year 1932-1933 (first series) averaged 0.677 and ranged between 0.66 and 0.69 except for three observations. The average error in estimating the value for oxygen consumption and for carbon dioxide production was — 3.0 and — 1.7 per cent, respectively. The number of calories dissipated by the alcohol flame in these checks averaged 23.27 per hour.

SUBJECTS

Twenty-two infants were studied. In the first series five were girls and seven boys; in the second series all ten infants were boys. Six infants were twins. The clinical criteria of the prematurity of the infants are given in table 2. The degree of prematurity, as estimated from the expected date of birth (obtained from the mother's history), varied from two weeks to three months, but because of the unreliability of this index, greater emphasis was assigned to the weight at birth, which ranged from 1,440 to 2,250 Gm., and to the height at birth, which was less than 45 cm. except for one infant (table 2).

The age at which the infants were first studied varied from one to sixty-four days. From two to nine observations were made on all infants except four (S. and J. in the first series and A. and R. in the second series; table 3), on whom single observations were made.

RESULTS

The detailed calorimetric data of the sixty-four observations are given in table 3 in terms of averages per hour. A summary of the results is presented in table 4, the infants in each series being listed according to the average age of each during the period of observation. All averages in this table and subsequent ones are weighted.

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9. Richardson, H. B.: Respiratory Quotient, Physiol. Rev. **9**:61, 1929.
10. Protein (grams) = urinary nitrogen (grams) $\times$ 6.25.

Basal Metabolism.—The basal metabolism of the twenty-two infants averaged 114 calories per twenty-four hours, ranging from 62 calories for an infant of 3 days weighing 1,312 Gm. to 184 calories for an infant of 67 days weighing 2,920 Gm. (table 4).

The average heat production for the twelve infants in the first series was 58.3 calories per kilogram of body weight per twenty-four hours, the range being from 44.6 to 74 (table 4). For the ten infants in the second series the average was 57.5 calories, but the range was

TABLE 2.—*Clinical Criteria of the Prematurity of the Infants Studied* *

Subject	Date of Birth	Expected Date of Birth	Weight at Birth, Gm.
First Series			
S. (female)	1/12/33	3/25/33	2,080
D. (female)	1/14/33	3/18/33	1,885
M.	2/12/33	3/ 1/33	1,530
R. (twin)	2/15/33	4/27/33	1,440
H. (female)	4/ 3/33	5/ 8/33	2,142
A.	4/ 8/33	6/ 8/33	2,000
J.	5/ 7/33	?	1,450
R. C. (twin)	4/21/33	6/21/33 (?)	1.575 (?)
L. C. (female, twin)	4/21/33	6/21/33 (?)	1.575 (?)
O'N.	6/ 4/33	6/17/33	2,250
M. (female, twin)	6/14/33	8/ 1/33	1,830
Mc.	6/17/33	8/17/33 (?)	2,010
Second Series			
P. C.	4/ 5/34	5/10/34 (?)	1,680
K. (twin)	10/26/34	12/ 7/34	1,925
J. M.	11/21/34	12/12/34	1,964
W.	12/ 7/34	1/22/35	1,813
C. W. (twin)	12/31/34	1/22/35	2,130
A. N.	1/ 7/35	3/ 2/35	1,910
A.	1/24/35	2/ 5/35	1,955
R. (died at 7 days of age)	2/ 4/35	4/ 1/35	1,520
B.	1/31/35	3/ 2/35	1,970
E. H.	3/11/35	6/ ?/35	1,620

* All the infants were born in the Woman's Clinic and were observed from birth except R. C. and L. C., who were admitted to the Children's Clinic at the age of 3 weeks, weighing approximately 1,100 Gm. each. All the infants except O'N. measured less than 45 cm. in length at birth.

smaller (from 47.2 to 63.9) because of technical improvements in the apparatus and the rigid control of environmental temperature and humidity. The weighted average for the whole group of twenty-two infants was 57.9 calories per kilogram, the coefficient of variability ($\frac{\text{standard deviation}}{\text{mean}}$) being 11 per cent (table 5). This order of variation compares favorably with the value derived by Murlin and his co-workers [6b] from a statistical analysis of his results for full term infants (13 per cent).

When referred to body surface, the basal metabolism averaged 743 calories per square meter per twenty-four hours (30.9 calories per hour), ranging from 538 to 862 calories for the whole group (table 4).

TABLE 3.—*Calorimetric Data in Averages per Hour*

Subject	Date	Observation	Duration of Observation, Minutes	Number of Periods	Age, Days	Weight, Gm.	Height, Cm.	Surface Area, Sq. Meters*	Water, Gm.	Carbon Dioxide, Gm.	Oxygen, Gm.	Respiratory Quotient, Total	Nitrogen in Urine, Gm.	Calories†	Daily Diet, Calories per Kg.‡	Last Meal, Calories per Kg.	Minutes After Meal	Average Rectal Temperature C.	Average Rectal Temperature F.	Average Temperature of Chamber, C.	Average Relative Humidity of Chamber, Percentage	Comments§
First Series																						
S.	1/24/33	177	120	2	12	2,112	44.0	0.1616	.....	1.76	1.42	0.901	.....	4.86	126	15	21	37.0	98.60	27.41	..	
D.	1/31/33	179	120	2	17	1,961	45.0	0.1530	.....	1.77	1.47	0.879	.....	4.99	136	15	31	36.8	98.24	27.51	..	
	2/ 3/33	181	180	3	20	2,100	45.0	0.1609	.....	2.02	....	.....	.....	5.42‖	140	18	32	36.5	97.70	27.29	..	Awake 20 min., cried 1 min.
M.	2/14/33	184	120	2	2	1,522	43.5	0.1264	.....	1.08	....	.....	.....	2.99¶	105	7	43	35.9	96.62	27.85	..	
	2/15/33	185	120	2	3	1,522	43.5	0.1264	.....	0.96	....	.....	.....	2.67¶	105	7	43	36.2	97.16	27.82	..	
R.	3/28/33	188	60	1	31	1,650	43.0	0.1343	.....	1.42	1.14	0.906	.....	3.91	162	8	41	36.9	98.42	25.42	..	
	3/29/33	189	120	2	32	1,680	43.0	0.1361	.....	1.58	1.25	0.925	.....	4.28	159	15	52	36.9	98.42	24.81	..	
H.	4/ 4/33	191	93	2	1	2,134	44.0	0.1629	.....	1.64	....	0.908	.....	4.47#	75	6	34	36.8	98.24	24.64	..	
	4/ 5/33	192	60	1	2	2,040	44.0	0.1575	.....	1.51	1.25	0.879	.....	4.26	91	10	36	36.8	98.24	25.03	..	
	4/ 7/33	193	110	2	4	2,100	44.0	0.1609	.....	1.61	1.31	0.894	.....	4.48	101	10	49	37.1	98.78	25.10	..	
	4/15/33	196	60	1	12	2,280	44.0	0.1712	.....	1.78	1.51	0.857	.....	5.12	152	12	52	37.5	99.50	25.12	..	
	4/29/33	200	95	2	26	2,880	....	0.2039	.....	2.45	....	.....	.....	7.08‖	128	7	44	37.4	99.32	27.19	..	Cried 2 min.
A.	4/12/33	195	60	1	4	1,888	42.5	0.1486	.....	1.60	....	.....	.....	4.52‖	85	10	81	36.5	97.70	26.58	..	Awake 1 min.
	4/18/33	197	60	1	10	1,974	42.5	0.1536	.....	1.90	1.61	0.858	.....	5.46	138	10	55	36.8	98.24	24.85	..	
	4/25/33	199	60	1	17	2,130	....	0.1626	.....	2.23	1.79	0.906	.....	6.14	128	10	72	36.9	98.42	26.43	..	Awake 1 min.
J.	5/ 9/33	202	120	2	2	1,364	39.5	0.1164	.....	1.24	....	0.949	.....	3.29#	9	8	60	35.9	96.62	25.60	..	Awake 46 min.
R. C.	5/10/33	203	120	2	19	1,200	39.5	0.1058	.....	1.33	1.01	0.958	.....	3.56	144	18	70	36.3	97.34	25.59	..	Awake 32 min.
	5/17/33	206	120	2	26	1,340	39.5	0.1149	.....	1.60	....	.....	.....	4.28‖	155	17	36	36.3	97.34	25.32	..	
L. C.	5/12/33	204	105	2	21	1,224	40.5	0.1073	.....	1.23	1.00	0.894	.....	3.42	87	11	60	35.9	96.62	26.18	..	
	5/16/33	205	60	1	25	1,320	40.5	0.1136	.....	1.40	1.10	0.926	.....	3.79	139	17	110	36.6	97.88	27.17	..	
O'N.	6/ 6/33	208	60	1	2	2,200	48.3	0.1666	.....	1.44	1.21	0.866	.....	4.11	**	9	57	37.3	99.14	26.62	..	
	6/23/33	217	91	2	19	2,632	49.2	0.1907	.....	2.29	....	.....	.....	6.53‖	110	8	38	36.9	98.42	26.43	..	Awake 19 min.
M.	6/16/33	212	120	2	2	1,746	43.0	0.1401	.....	1.20	1.09	0.865	.....	3.44#	9	4	75	36.7	98.06	26.45	..	Cried 1 min.
	6/27/33	219	100	2	13	1,902	44.0	0.1494	.....	1.49	1.15	0.948	.....	3.97	126	11	63	35.9	96.62	27.42	..	
Mc	6/21/33	216	60	1	4	1,950	44.2	0.1522	.....	1.70	1.46	0.847	.....	4.93	82	10	60	37.1	98.78	26.36	..	
	6/30/33	220	45	1	13	2,136	45.0	0.1630	.....	1.91	....	.....	.....	5.33‖	114	9	59	36.7	98.06	28.47	..	
Second Series																						
P. C.	6/ 8/34	P 1	60	1	64	2,870	49.0	0.2025	2.884	2.839	2.159	0.956	.....	7.50	140	23	50	37.0	98.60	26.05	43	
	6/14/34	P 2	160	3	70	2,970	50.5	0.2075	3.372	2.906	2.262	0.934	0.0169	7.83	135	22	42	37.2	98.96	26.25	58	

K.	11/ 3/34	P 6	116	3	8	1,926	44.0	0.1480	3.440	1.543	1.237	0.907	0.0078	4.26	131	16	51	36.2	97.16	26.99	53	Cried 3 min.
	11/16/34	P 7	105	3	21	2,266	46.0	0.1675	2.638	1.676	1.334	0.910	0.0239	4.56	116	16	59	36.2	97.16	25.72	37	
	11/19/34	P 8	78	2	24	2,304	46.0	0.1700	2.825	1.986	1.573	0.918	.....	5.40	119	13	80	36.3	97.34	28.46	33	
	11/21/34	P 9	107	3	26	2,322	46.5	0.1720	3.142	2.034	1.538	0.962	.....	5.35	119	16	63	36.6	97.88	28.08	38	
	11/22/34	P10	125	3	27	2,354	46.5	0.1725	3.148	2,076	1.670	0.904	0.0199	5.73	117	16	58	37.0	98.60	26.61	41	
J. M.	12/ 4/34	P11	40	1	14	1,968	45.0	0.1515	2.608	1.941	1.511	0.935	0.0088	5.23	136	17	91	36.6	97.88	27.92	38	
	12/ 6/34	P12	73	2	16	2,064	45.0	0.1550	2.324	1.777	1.350	0.958	.....	4.70	129	17	83	36.9	98.42	28.22	35	
	12/18/34	P18	89	2	28	2,404	46.0	0.1760	2.718	2.098	1.781	0.857	0.0291	6.02	121	14	51	36.9	98.42	28.27	42	
C. W.	12/10/34	P13	77	2	3	1,776	43.5	0.1425	2.637	1.528	1.260	0.882	.....	4.31	90	11	59	36.2	97.16	27.95	46	
	12/12/34	P15	86	2	5	1,754	43.5	0.1400	2.538	1.441	1.224	0.857	0.0049	4.17	122	13	82	36.2	97.16	27.88	42	
	12/13/34	P16	116	3	6	1,730	43.5	0.1390	2.507	1.499	1.281	0.852	.....	4.35	123	13	60	36.2	97.16	27.62	44	
	12/17/34	P17	78	2	10	1,800	44.0	0.1435	2.462	1.630	1.370	0.865	0.0071	4.67	119	15	57	37.0	98.60	28.11	42	
	12/31/34	P19	91	2	24	2,214	45.0	0.1650	2.733	1.828	1.460	0.911	0.0101	5.03	123	12	60	37.1	98.78	28.13	46	Awake 8 min.; awake, restless, 10 min.
W.	1/ 8/35	P23	28	1	8	2,210	45.0	0.1650	2.226	1.601	1.339	0.869	0.0058	4.56	115	12	103	36.9	98.42	28.11	37	
	1/ 9/35	P24	75	2	9	2,210	45.0	0.1650	2.443	1.989	1.690	0.856	0.0088	5.74	121	15	60	37.0	98.60	28.43	43	Awake, restless, 2 min.
	1/22/35	P26	111	3	22	2,560	47.0	0.1855	3.122	2.486	2.067	0.875	.....	7.06	121	16	48	37.3	99.14	28.74	47	Awake, restless, 8 min.
A. N.	1/16/35	P25	97	2	9	1,816	43.0	0.1435	2.819	1.630	1.322	0.896	0.0083	4.54	117	15	47	36.5	97.70	27.24	52	
	1/23/35	P27	79	2	16	1,948	44.0	0.1500	2.350	1.761	1.374	0.932	.....	4.76	130	17	47	36.4	97.52	27.53	39	
	1/28/35	P28	86	2	21	2,128	45.0	0.1610	2.417	1.843	1.450	0.924	.....	5.02	125	16	57	36.7	98.06	27.66	40	
	1/29/35	P29	80	2	22	2,136	45.0	0.1610	2.524	1.800	1.394	0.939	.....	4.84	125	16	59	36.6	97.88	27.57	34	
	2/14/35	P35	75	2	38	2,580	47.0	0.1865	2.938	2.064	1.724	0.871	0.0072	5.88	117	17	67	37.3	99.14	28.52	37	
	2/19/35	P37	70	2	43	2,720	48.0	0.1945	3.115	2.307	1.874	0.895	0.0077	6.43	117	17	54	37.3	99.14	28.02	45	
A.	1/31/35	P30	36	1	7	2,034	46.0	0.1550	2.448	1.667	1.312	0.924	0.0220	4.51	105	11	100	36.5	97.70	27.79	35	Cried 2 min.
R.	2/ 7/35	P34	60	1	3	1,312	40.0	0.1120	.....	0.821	0.779	0.767	.....	2.58	61	8	55	35.0	95.00	27.07	31	
B.	3/ 5/35	P39	83	2	34	2,160	48.0	0.1625	2.786	2.117	1.591	0.968	.....	5.76	124	16	68	37.3	99.14	28.72	36	Awake, restless, 4 min.
	3/ 7/35	P40	94	2	36	2,286	48.0	0.1700	2.746	2.182	1.721	0.922	0.0153	5.94	128	16	50	36.8	98.24	27.60	38	Awake, restless, 7 min.
	3/ 8/35	P41	102	2	37	2,386	48.0	0.1750	3.189	2.399	1.881	0.928	0.0144	6.50	128	17	56	36.9	98.42	28.73	41	
H.	3/14/35	P42	104	2	3	1,560	40.5	0.1290	.....	1.333	1.079	0.898	.....	3.69	103	13	64	36.6	97.88	27.99	35	
	3/15/35	P43	92	2	4	1,560	40.5	0.1290	.....	1.397	1.118	0.909	0.0106	3.84	103	13	51	36.8	98.24	28.01	35	Cried 1 min.
	3/25/35	P44	46	1	14	1,800	42.0	0.1435	2.473	1.676	1.274	0.957	.....	4.43	140	14	45	37.0	98.60	28.08	34	
	3/28/35	P45	84	2	17	1,880	42.0	0.1475	2.569	1.939	1.378	1.024	0.0122	5.33‖	142	17	51	36.8	98.24	28.20	35	
	3/29/35	P46	97	2	18	1,940	42.0	0.1500	2.598	1.918	1.433	0.973	0.0149	5.19‖	136	17	60	36.7	98.06	28.45	32	
	4/22/35	P48	118	2	42	2,600	46.0	0.1875	3.305	2.332	1.905	0.890	0.0134	6.53	115	19	56	37.3	99.14	28.81	43	
	4/29/35	P49	34	1	49	2,800	46.8	0.1980	3.626	2 301	1.895	0 883	0.0093	6.33	107	18	123	36.9	98.42	29.00	45	
	4/30/35	P50	34	1	50	2,880	46.8	0.2030	3.771	2.250	1.961	0.835	0.0129	6.30‖	125	15	123	37.3	99.14	28.81	50	
	5/16/35	P57	30	1	66	3,280	48.0	0.2300	4.476	2.730	2.120	0.937	0.0145	7.34	106	18	52	37.2	98.96	28.24	48	

* The surface area was calculated from the formula of Klein and Scammon ($5.188\ wt.^{0.750}$).[12]

† When the sample of urine was incomplete the number of calories was calculated in the first series on the assumption that 15 per cent were derived from protein and in the second series using the value for urinary nitrogen obtained for the same infant on the same diet in other observations.

‡ The daily diet consisted of breast milk except in observations P7 to P10, inclusive, and P18, in which a formula of evaporated milk was given. The meal just prior to the observation always consisted of breast milk.

§ The infant was asleep throughout and made only occasional movements of adjustment except as noted.

‖ Calculated from the amount of carbon dioxide eliminated, with the respiratory quotient obtained for the same infant under the same dietary conditions; the determination of the oxygen consumption was not satisfactory.

¶ Calculated from the amount of carbon dioxide eliminated at an assumed respiratory quotient of 0.9.

Calculated from the amount of carbon dioxide eliminated, with a satisfactory respiratory quotient obtained for only one period.

** Vomited all feedings on day prior to observation.

The coefficient of variability was 11.6 per cent, the same as that determined for the basal metabolism when referred to weight.[11] Surface area and weight[12] are thus equally reliable constants for reference of the basal metabolism of premature infants.

The basal metabolism when referred to body height varied from 1.55 to 3.70 calories per centimeter per twenty-four hours, the coefficient of variability being 20 per cent. The wide variation undoubtedly occurred because the average heights of the individual infants ranged from 39.5 to 49.7 cm. (table 4), a difference of only 26 per cent, whereas the average weights varied from 1,270 to 2,287 Gm., a difference of 80 per cent. This high order of variability and the known difficulties of measuring accurately the total length of premature infants suggest that this physical constant is less suitable than either body weight or body surface for reference of the basal metabolism.

As the age of the infant increased, the total number of calories increased, possibly because of the concomitant increase in body weight rather than because of the increased age per se. In calories per kilogram, individual infants in this small series showed no consistent trend within the range of ages studied (from 1 to 70 days). In chart 1 are presented curves showing the changes in basal metabolism of the five infants on whom five or more determinations were made. It may be seen that the number of calories per kilogram increased as the age of the infant increased for K. and H. and that for C. W., A. N. and E. H. there was no unidirectional change. In table 5 the mean numbers of calories per kilogram are arranged according to the ages of the infants, in weeks. The difference in the number of calories per kilogram for infants in the first week and for infants in the second week of postnatal life was 5.3 calories, or 3.3 times its probable error (±1.59). For the other age groups the difference was always less than twice its probable error.

11. This was anticipated, since the surface area was calculated from a formula based on body weight alone. The formula of Klein and Scammon ($5.188\ wt.^{0.750}$) was used because it fitted the measurements they made of fetal surface area more closely than the extension of the DuBois weight-height formula or their own formulas calculated from height, crown-rump length or height and weight together. The formula used by Marsh and Murlin[1a] ($10.3\ \sqrt[3]{wt.^2}$; Lissauer), by Schadow[1c] and by Talbot and his co-workers[1b] ($10\ \sqrt[3]{wt.^2}$; Benedict) gave a value for surface area which at the average weights of the infants studied by these three observers were 1.3, 2 and 3 per cent higher, respectively, than those obtained by application of the Klein and Scammon formula.

12. Klein, A. D., and Scammon, R. E.: Relations Between Surface Area, Weight and Length of the Human Body in Prenatal Life, Proc. Soc. Exper. Biol. & Med. **27**:456, 1930.

TABLE 4.—Summary of Results

TABLE 4.—*Summary of Results*

Subject	Number of Observations	Age, Days: Average Range	Weight, Gm.: Average Range	Height, Cm.: Average Range	Surface Area, Square Meters: Average Range	Calories per 24 Hours: Average Range	Calories per 24 Hours per Kg.: Average Range	Calories per 24 Hours per Cm.: Average Range	Calories per 24 Hours per Square Meter: Average Range	Daily Diet, Calories per Kg.: Average Range	Meal Just Prior to Observation, Calories per Kg.: Average Range	Beginning of Observation, Minutes After Meal: Average Range	Average Rectal Temperature C.	Average Rectal Temperature F.	Temperature of Chamber, C.: Average Range
First Series															
J.	1	2.0	1,364	39.5	0.1164	79	57.9	2.00	679	9	8	60	35.9	96.62	25.60
M.	2	2.5 (2- 3)	1,522 (1,522-1,522)	43.5 (43.5-43.5)	0.1264 (0.1264-0.1264)	68 (64- 72)	44.6 (42.1-47.1)	1.57 (1.47-1.66)	538 (506-570)	105 (105-105)	7 (7-7)	43 (43-43)	36.1	96.98	27.84 (27.82-27.85)
M.	2	7.5 (2-13)	1,824 (1,746-1,902)	43.5 (43.0-44.0)	0.1448 (0.1401-0.1494)	89 (83- 95)	48.7 (47.3-50.1)	2.05 (1.92-2.17)	614 (590-638)	68 (9-126)	8 (4-11)	69 (63-75)	36.3	97.34	26.93 (26.45-27.42)
Mc.	2	8.5 (4-13)	2,043 (1,950-2,136)	44.6 (44.2-45.0)	0.1576 (0.1522-0.1630)	123 (118-128)	60.3 (59.8-60.7)	2.76 (2.68-2.84)	780 (777-784)	97 (82-112)	10 (9-10)	60 (59-60)	36.9	98.42	27.42 (26.36-28.47)
H.	5	9.0 (1-26)	2,287 (2,040-2,880)	....	0.1713 (0.1575-0.2039)	122 (102-170)	52.9 (50.0-59.0)	....	704 (648-834)	109 (75-152)	9 (6-12)	45 (34-52)	37.1	98.78	25.47 (24.64-27.19)
A.	3	10.3 (4-17)	1,997 (1,888-2,130)	....	0.1549 (0.1486-0.1626)	129 (108-147)	64.3 (57.4-69.2)	....	828 (727-904)	117 (85-138)	10 (10-10)	69 (55-81)	36.7	98.06	25.96 (24.86-26.43)
O'N.	2	10.5 (2-19)	2,416 (2,200-2,632)	48.8 (48.3-49.2)	0.1787 (0.1666-0.1907)	128 (99-157)	52.2 (44.8-59.5)	2.62 (2.04-3.19)	708 (592-823)	55 (*-110)	9 (8-9)	48 (38-57)	37.1	98.78	26.53 (26.43-26.62)
S.	1	12.0	2,112	44.0	0.1616	117	55.2	2.66	724	126	15	21	37.0	98.60	27.41
D.	2	18.5 (17-20)	2,030 (1,961-2,100)	45.0 (45.0-45.0)	0.1570 (0.1530-0.1609)	125 (120-130)	61.5 (61.1-61.9)	2.78 (2.67-2.89)	796 (784-808)	138 (136-140)	17 (15-18)	32 (31-32)	36.7	98.06	26.38 (25.25-27.51)
R. C.	2	22.5 (19-26)	1,210 (1,200-1,340)	39.5 (39.5-39.5)	0.1104 (0.1058-0.1149)	94 (85-103)	74.0 (71.3-76.7)	2.38 (2.15-2.61)	850 (803-897)	149 (144-155)	18 (17-18)	53 (36-70)	36.3	97.34	25.46 (25.32-25.59)
L. C.	2	23.0 (21-25)	1,272 (1,224-1,320)	40.5 (40.5-40.5)	0.1105 (0.1073-0.1136)	87 (82- 91)	67.9 (67.0-68.9)	2.14 (2.03-2.25)	783 (765-801)	113 (87-139)	14 (11-17)	85 (60-110)	36.3	97.34	26.44 (26.18-26.69)
R.	2	31.5 (31-32)	1,665 (1,650-1,680)	43.0 (43.0-43.0)	0.1352 (0.1343-0.1361)	98 (94-102)	59.1 (56.9-61.2)	2.28* (2.19-2.37)	725 (700-750)	161 (159-162)	12 (8-15)	46 (41-52)	36.9	98.42	25.12 (24.81-25.43)
Average	26	13.2 (2-32)	1,817 (1,270-2,287)	43.2 (39.5-48.8)	0.1437 (0.1104-0.1787)	105 (68-129)	58.3 (44.6-74.0)	2.32 (1.57-2.78)	727 (538-850)	104 (9-161)	11 (7-18)	52 (21-85)	36.6	97.88	26.38 (25.12-27.84)
Second Series															
R.	1	3.0	1,312	40.0	0.1120	62	47.2	1.55	553	61	8	55	35.0	95.00	27.07
A.	1	7.0	2,034	46.0	0.1550	109	53.3	2.36	700	105	11	100	36.5	97.70	27.79
C. W.	5	9.6 (3-24)	1,855 (1,730-2,214)	43.9 (43.5-45.0)	0.1460 (0.1390-0.1650)	108 (100-121)	58.6 (54.5-62.3)	2.46 (2.30-2.68)	741 (715-781)	116 (90-123)	13 (11-15)	64 (59-82)	36.6	97.88	27.94 (27.61-28.13)
W.	3	13.0 (8-22)	2,327 (2,210-2,560)	45.7 (45.0-47.0)	0.1718 (0.1650-0.1855)	139 (109-169)	59.3 (49.5-66.2)	3.03 (2.43-3.61)	803 (663-913)	119 (115-121)	14 (12-16)	70 (48-103)	37.1	98.78	28.42 (28.11-28.73)
J. M.	3	19.3 (14-28)	2,145 (1,968-2,404)	45.3 (45.0-46.0)	0.1608 (0.1515-0.1760)	128 (113-144)	59.5 (54.7-63.8)	2.81 (2.51-3.14)	792 (728-828)	129 (121-136)	16 (14-17)	75 (51-91)	36.8	98.24	28.16 (27.99-28.27)
K.	5	21.2 (8-27)	2,234 (1,926-2,354)	45.8 (44.0-46.5)	0.1660 (0.1480-0.1725)	121 (102-137)	54.3 (48.3-58.3)	2.64 (2.31-2.95)	730 (653-796)	120 (116-131)	15 (13-16)	62 (51-80)	36.5	97.70	27.17 (25.72-28.46)
A. N.	6	24.8 (9-43)	2,221 (1,816-2,720)	45.3 (43.0-48.0)	0.1658 (0.1435-0.1945)	126 (109-154)	57.0 (54.7-60.0)	2.78 (2.53-3.21)	760 (733-793)	122 (117-130)	16 (15-17)	55 (47-67)	36.9	98.42	27.76 (27.24-28.52)
E. H.	9	29.2 (3-66)	2,287 (1,560-3,380)	43.8 (40.5-48.0)	0.1686 (0.1290-0.2300)	131 (89-176)	58.5 (52.1-68.0)	2.94 (2.19-3.67)	773 (687-867)	120 (103-142)	16 (13-19)	70 (45-123)	37.0	98.60	28.39 (27.99-29.00)
B.	3	35.7 (34-37)	2,277 (2,160-2,386)	48.0 (48.0-48.0)	0.1688 (0.1615-0.1750)	146 (138-156)	63.9 (62.4-65.4)	3.03 (2.88-3.27)	869 (839-891)	127 (124-128)	16 (16-17)	58 (50-68)	36.8	98.24	28.35 (27.60-28.73)
P. C.	2	67.0 (64-70)	2,920 (2,870-2,970)	49.7 (49.0-50.5)	0.2050 (0.2025-0.2075)	184 (180-188)	63.0 (62.7-63.3)	3.70 (3.67-3.72)	897 (888-906)	138 (135-140)	23 (22-23)	46 (42-50)	37.1	98.78	26.15 (26.05-26.25)
Average	38	23.0 (3-67)	2,159 (1,312-2,920)	45.4 (40.0-49.7)	0.1620 (0.1120-0.2050)	125 (62-184)	57.5 (47.2-63.9)	2.73 (1.55-3.70)	762 (553-862)	116 (61-138)	15 (8-23)	65 (46-100)	36.6	97.88	27.73 (26.15-28.39)
Total average	**64**	**17.6 (1-70)**	**1,972 (1,270-2,287)**	**44.3 (39.5-49.7)**	**0.1520 (0.1104-0.2050)**	**114 (62-184)**	**57.9 (44.6-74.0)**	**2.53 (1.55-3.70)**	**743 (538-862)**	**109 (9-161)**	**13 (7-23)**	**58 (21-100)**	**36.6**	**97.88**	**27.00 (25.12-28.39)**

* Vomited all feedings on day prior to observation.

The calculation of the weighted averages for ten full term infants, grouped according to age in weeks and studied during the first month by Marine and his co-workers,[6a] likewise shows that the lowest metabolism in calories per kilogram occurred during the first week (46), with a rise from the first to the second week of 3.7 calories and from the second to the third week of 3.6 calories. Both these differences were less than three times their respective probable errors, but the

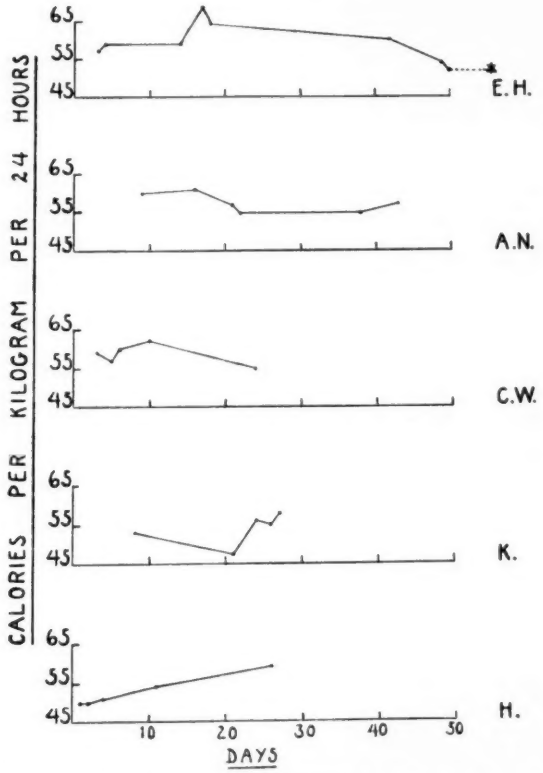

Chart 1.—Curves showing the effect of increasing age on the basal metabolism of five premature infants expressed in calories per kilogram per twenty-four hours. At the end of the upper curve * indicates 66 days.

combined rise of 7.3 calories from the first to the third week was approximately six times its probable error.

This increase in metabolism occurring in both premature and full term infants during the second and third weeks of life may be related either to an increase in food intake or to a more fundamental adjustment to changes in internal or external milieu. Direct evidence is not at present available for adjudging the respective merits of these theoretical considerations.

Statistical Analysis of Results.—Statistical evidence that weight and surface area are better adapted for reference of basal metabolism in premature infants than height and age is presented in table 6, in which the coefficients and partial coefficients [13] of correlation between metabolism and these physical factors are given.[14]

The high coefficients of correlation between metabolism and weight (0.89 ± .02) or surface area (0.90 ± .02) exceed those for age

TABLE 5.—*Metabolism of Premature Infants in Calories per Kilogram per Twenty-Four Hours, According to Age Groups*

Age, Days	Number of Infants	Number of Observations	Mean Number of Calories per Kg. per 24 Hours	Probable Error of Mean
1- 7	11	17	52.8	1.237
8-14	11	12	58.1	1.004
15-21	9	12	62.0	1.698
22-28	8	10	62.1	1.868
29-70	5	13	59.2	1.211
Total	22	64	57.9*	0.938

* Coefficient of variability, 11 per cent.

TABLE 6.—*Coefficients of Correlation* *

Variables	Number of Observations	Coefficients of Correlation
Weight		
Height	41	0.92843 ± 0.01490
Age	44	0.53363 ± 0.07443
Basal metabolism		
Age	44	0.65400 ± 0.05956
Weight	44	0.88683 ± 0.02222
Height	41	0.77375 ± 0.04334
Surface area	44	0.89067 ± 0.01983
Partial Coefficients of Correlation		
Basal Metabolism		
Weight : age†	44	0.84066 ± 0.03089
Weight : height	41‡	0.69886 ± 0.05597
Height : weight	41‡	−0.26312 ± 0.10184
Age : weight	44	0.46255 ± 0.08280

* For this analysis the observations were arbitrarily divided according to the age of the infants in weeks.

† The factor following the colon is the variable held constant in each of the calculations.

‡ In calculating these coefficients, the coefficient between the metabolism and the weight used was 0.88284 ± 0.02382, determined for forty-one observations, instead of the coefficient previously determined for forty-four observations.

(0.65 ± .06) or height (0.77 ± .04) and attest to the close relationship between metabolism and weight or surface area. The high par-

13. These coefficients were calculated in the usual manner. Inclusion of the factor of age in the partial coefficients is not strictly valid, since its relation to basal metabolism and weight within the range studied is nonlinear.

14. Pearl, R.: Medical Biometry and Statistics, Philadelphia, W. B. Saunders Company, 1923. Dunn, H. L.: Application of Statistical Methods in Physiology, Physiol. Rev. **9**:275, 1929.

tial coefficients between metabolism and weight [15] with age or height held constant ($0.84 \pm .03$ and $0.70 \pm .06$), and conversely (*a*) the lack of significant correlation between metabolism and height ($-0.26 \pm .10$) and (*b*) the relatively low correlation between metabolism and age ($0.46 \pm .08$) with weight held constant in both instances demonstrate the importance of weight as a determinant of metabolism in premature infants.

That the relatively high coefficients of correlation between basal metabolism and height or age ($0.77 \pm .04$ and $0.65 \pm .06$, respectively) were to a large extent due to coincidental changes in weight is suggested by the correlations between weight and height or age ($0.93 \pm .01$ and

TABLE 7.—*Average Respiratory Quotients*

	Less Than 9 Days Old			More Than 9 Days Old			Total		
Series	Number of Infants	Number of Observations		Number of Infants	Number of Observations		Number of Infants	Number of Observations	
1	5	7	0.884 (0.842-0.949)	8	11	0.909 (0.876-0.958)	11	18	0.899
2	5	11	0.867 (0.767-0.907)	8	27	0.913 (0.866-0.945)	10	38	0.900
Total	10	18		16	38		21	56	
Average			0.876			0.911			0.899

TABLE 8.—*Percentage of Calories Derived from Protein*

Daily Diet	Meal Just Prior to Observation	Number of Infants	Number of Observations	Percentage of Calories Derived from Protein	
				Average	Range
Human milk	Human milk	8	30	4.9	2.7-7.9*
Cow's milk	Human milk	3	4	11.1	8.5-13.9
Cow's milk	Cow's milk	1	1	16.6	

* In a single observation on one infant (P30, table 3), the percentage of calories derived from protein was 10.6.

$0.53 \pm .07$). The partial coefficients of correlation between metabolism and height or age with weight held constant were, as previously mentioned, of a lower order.

Respiratory Quotients and Protein Metabolism.—The average respiratory quotient for all except two of twenty-one infants (R. C. and R.) varied from 0.87 to 0.95 and averaged 0.90 (table 7). The average respiratory quotient for infants less than 9 days old averaged 0.88 and for those older than 9 days, 0.91. The lowest respiratory quotient, 0.77, was obtained in an infant 3 days old (R), who had

15. Since the surface area was calculated from a weight formula alone, it was presumed that no further information would be gained by determining its partial coefficients.

ingested little during the two days prior to the observation. The average respiratory quotient, 0.88, obtained for the infants less than 9 days old (0.89, if this infant is omitted) suggests that they can oxidize the lactose of breast milk as readily as older premature infants.

The percentage of calories [16] derived from protein [17] in thirty observations on eight infants who were fed breast milk solely averaged 4.9 per cent and ranged from 2.7 to 7.9 per cent except for one observation, in which it was 10.6 per cent (P30, table 3).

The average proportion of calories derived from protein in four observations on infants who were fed cow's milk as their daily diet but breast milk in the meal just prior to the observations was 11.1 per cent, the proportion for individual infants ranging from 8.5 to 13.9 per cent (table 8). In a single observation on an infant who received cow's milk in the preceding meal as well as in the daily diet, 16.6 per cent of the calories were derived from protein (not shown in table 3). This figure is within the range found for older full term infants on a diet of cow's milk.[18] Further studies on the utilization of the protein of cow's milk by premature infants are in progress.

COMMENT

The basal metabolism (total calories) of the premature infants studied, as might have been expected from their small size, was less than that of full term infants of the same postnatal age. For purposes of comparison, body weight and surface were found to be the most suitable constants for reference of the basal metabolism.[19]

Marsh and Murlin [1a] found that expressed in calories per kilogram the basal metabolism of premature infants during the first two weeks of life was practically the same as that of full term infants of comparable age. Schadow,[1c] similarly, found for premature infants over 2 weeks of

16. The calories derived from protein were calculated in the customary manner, by multiplying the urinary nitrogen, in grams, by 26.51 (table 3, second series only, as shown by Lusk).

17. Lusk, G.: Science of Nutrition, ed. 3, Philadelphia, W. B. Saunders Company, 1923, p. 62.

18. Levine, S. Z.; Wilson, J. R., and Gottschall, G.: The Respiratory Metabolism in Infancy and in Childhood: X. The Respiratory Exchange in Marasmus; Specific Dynamic Action of Food in Normal and in Marasmic Infants, Am. J. Dis. Child. **36**:740 (Oct.) 1928.

19. Statistical analysis showed that weight and surface area are equally reliable. The number of direct measurements of the surface area of premature and full term infants is small, and until more measurements are available it seems desirable to employ both physical constants, with more emphasis laid for the time being on body weight than on estimations of surface area calculated from formulas based on weight.

age deviations in the number of calories per kilogram during the first, second and third months of life of only —9, —4 and +4 per cent, respectively, from the figures secured under comparable conditions for full term infants.[20] Comparison of the figures of Talbot and his co-workers [1b] with those of Benedict and Talbot [6d] demonstrated that for similar age groups the metabolism of premature and full term infants expressed in calories per kilogram is practically identical. Finally, our average figure of 58 calories per kilogram per twenty-four hours compares favorably with the basal metabolic rate previously reported from this laboratory for full term infants during the first year of life.[21] The published evidence and the material presented in this paper are thus in accord in demonstrating that the basal rate of heat production of premature infants is at least as high as that of full term infants when referred to body weight.

When referred to surface area, the basal metabolic rate of premature infants is lower than that of full term infants. This is shown in chart 2, in which the results of forty-four observations on the premature infants under discussion and forty-one observations on older full term infants previously studied in this laboratory are plotted in calories per square meter and calories per kilogram against body weight. With increasing weight there is a marked increase in calories per square meter, without a coincidental change in calories per kilogram. The superimposed curves of Benedict and Talbot [6d] derived from a study of full term infants show a similar relationship, although at a lower level. This definite tendency at the age of the infants studied for the basal metabolic rate in calories per square meter to vary inversely with body weight raises the question, perhaps philosophical, whether one should attribute to premature infants an inherent peculiarity in metabolism or ascribe the defect to an anatomic fact, the relative disproportion in smaller infants between surface area and mass of heat-producing tissues.

The tendency to hypothermia may be explained by either of these concepts. In accord with the latter are the clinical impression that smaller infants require more clothes to maintain their normal body temperature and the experimental observations of Blackfan and Yaglou [5] that under the same rigidly controlled atmospheric conditions larger infants have less tendency to a subnormal temperature. Further

20. The use of phenobarbital sodium as a sedative in apparently the same absolute dose (from 30 to 50 mg., subcutaneously) for both premature and full term infants may have helped cause the slight negative deviations (Schadow, H.: Grundumsatz und spezifisch-dynamische Wirkung bei gesunden Säuglingen im Vergleich mit den Befunden bei Erwachsenen und älteren Kindern, Jahrb. f. Kinderh. **126**:50, 1929; footnote 1c).

21. Levine and others.[3c] Levine and Marples.[6f]

support of this view is lent by the results of Mordhorst,[2d] who found that the exposure of premature and full term infants to comparable cooling resulted in a low rectal temperature more frequently in the premature infants, although their average heat production had been increased 45 per cent, as compared with 28 per cent for the full term infants.

Further investigations of the mechanisms of heat loss are obviously needed. If it should be found that the loss of heat per unit of body surface in premature infants does not vary appreciably from that in full term infants under comparable varying experimental conditions, then

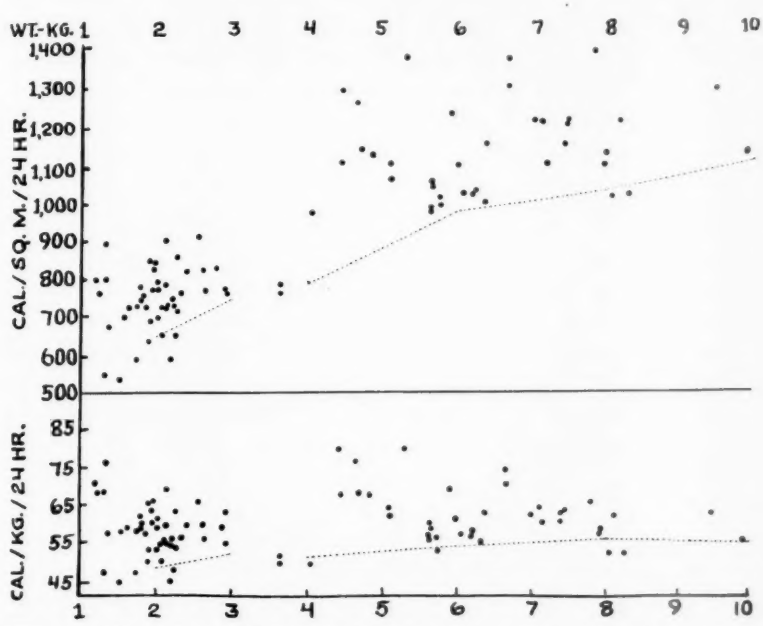

Chart 2.—The effect of increasing weight on the basal metabolism of premature and full term infants when referred to body weight and body surface. The dots show our observations; the dashes, the curve derived by Benedict and Talbot for full term infants. (Talbot and others [1b]; Levine and others [6e]).

stimulation of the heat production of the former, by a high caloric diet or administration of calorigenic endocrine products, to a level approximating in calories per square meter that of full term infants might lessen the tendency to subnormal temperatures.

A comparison of our results for premature infants with those of Marsh and Murlin,[1a] Schadow [1c] and Talbot and his co-workers [1b] shows that expressed in calories per kilogram our determinations exceeded theirs by 9, 20 and 22 per cent, respectively. These dis-

crepancies possibly may be explained by differences in (*a*) the technic used in the observations, (*b*) the environmental and rectal temperatures of the subjects, (*c*) their nutriment and (*d*) their activity.

The use of a small chamber in an air-conditioned suite afforded optimal conditions in our second series of observations, whereas the first observations were performed under experimental conditions comparable to those of earlier investigators. The similarity between the average number of calories per kilogram in the two series (58.3 and 57.5) suggests that the improvements in the technic of measurement in the second series do not explain the differences between our results and those previously reported. Furthermore, modifications in technic which serve to minimize the effect of environmental fluctuations hardly explain a unidirectional deviation.

The environmental temperature during observations was approximately the same in the different investigations, the average temperature in all being between 26 and 29 C. Rectal temperatures likewise were similar, being normal in the great majority of instances.

The difference of 9 per cent between our results for premature infants during the first two weeks of life and those of Marsh and Murlin may be explicable by differences in nutriment. Although the caloric content of the meal just prior to the observation was practically the same for their observations as for ours,[22] the low average respiratory quotient for their series, 0.79, as compared with 0.88 for our infants, suggests that our infants were either assimilating their food better or that their daily dietary was higher in carbohydrate. The percentage of carbohydrate cannot be calculated from the published data.

The difference of 20 per cent between our results and those of Schadow for premature infants of comparable ages may possibly be attributable to (*a*) the administration by that investigator of from 30 to 50 mg. of phenobarbital sodium hypodermically to assure rest in place of the customary small meal given by American investigators and (*b*) the fact that the daily caloric intake of his infants averaged 110 calories per kilogram as compared to 130 calories per kilogram for the infants in our investigation. Both factors may have contributed to the lower rate of heat production of his infants.

The difference of 22 per cent between our results and those of Talbot may be explicable by differences in the daily feeding schedules or in the caloric content of the meal given just prior to the observation. The published data are inadequate for assessment of these factors. Use of the value for the amount of carbon dioxide eliminated to calculate the rate of heat production at the average respiratory quotient of 0.96,

22. For those infants in the series of Murlin and Marsh for whom the data permit calculation, the meals averaged from 10 to 11 calories per kilogram.

obtained in twenty-two of fifty-one observations reported by Talbot and assumed for the remainder, would in itself, wherever used, introduce an error of 5 per cent if the average respiratory quotient of 0.91 obtained in this study were substituted.[6c]

An unequivocal explanation of the discrepancies between the results given in the published reports and our results is obviously not at hand, since the available data do not permit a precise appraisal of the various factors discussed. It may be of some practical import to determine by carefully controlled observations the effect of a high caloric diet and of the use of uncovered cribs in a nursery with a constant temperature and humidity on the metabolism of premature infants. It is at least conceivable that either or both of these factors were associated with the higher metabolism determined for our infants.

SUMMARY

The basal metabolism of twenty-two premature infants, ranging in age from 1 to 70 days and in weight from 1,200 to 3,380 Gm., was determined under controlled conditions of diet and environment. The use of a small respiratory chamber in which dead air space was reduced to a minimum, refinements in the technic of measurements and rigid control of environmental conditions during observations permitted a satisfactory series of alcohol checks, which attested the reliability of observations at a level of heat production comparable to that of the infants (from 3 to 8 calories per hour).

The number of basal calories per twenty-four hours produced by premature infants, as might be expected from their small size, was less than that of full term infants of the same postnatal age.

In terms of body weight the basal metabolic rate averaged 58 calories per kilogram per twenty-four hours. The only statistically significant change in the number of calories per kilogram from week to week within the age range studied was an increase of 5.3 calories from the first to the second week of postnatal life. Our results exceed those found by other investigators, but all authors are in accord that when referred to body weight the basal metabolic rate of premature infants is similar to that of full term infants of a comparable age.

When referred to body surface the rate is lower in premature infants. This may be explained either by their larger surface area in proportion to their body weight or by the assumption of an inherent defect in heat production.

A statistical analysis of the results supports the choice of body weight or surface area as a reliable constant for the reference of the basal metabolic rate of premature infants. Within the range of ages studied the highest coefficients of correlation existed between heat

production and weight ($0.89 \pm .02$) or surface area ($0.90 \pm .02$), as compared to the correlation for heat production and height ($0.77 \pm .04$) or age ($0.65 \pm .06$).

The respiratory quotient of 0.88 obtained during the first week of life suggests that when given adequate amounts of carbohydrate (lactose) premature infants can readily metabolize it. The nitrogen content of the urine collected during short periods for the premature infants fed breast milk only was low and represented only 4.9 per cent of the total number of calories produced.

CONCLUSIONS

The basal metabolic rate of premature infants expressed in calories per kilogram closely approximates and in calories per square meter is less than that of full term infants of a comparable age. The low metabolic rate of premature infants when referred to surface area may represent an intrinsic abnormality of heat production or may be ascribable to an anatomic fact, namely, the larger surface area in relation to the mass of heat-producing tissues. An assessment of the relative importance of these factors in the origin of the hypothermia of premature infants must await comparative studies in premature and full term infants of the loss as well as the production of heat under environmental conditions which burden the mechanisms regulating body temperature.

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ESTIMATION OF VITAMIN D IN BLOOD SERUM

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A method of determining the vitamin D content of the blood serum is desirable in the diagnosis and treatment of rickets and other disturbances of mineral metabolism and maladies of the bones. Clinical and roentgenologic signs are not always sufficient. Chemical methods may be helpful, the best known and most widely employed being estimation of the inorganic phosphorus content of the blood. Variations in the inorganic phosphorus content and the blood phosphatase level (the determination of which has recently been recommended) are not specific for rickets, since these changes may result from a variety of pathologic conditions. A direct estimation of the vitamin D content of the blood serum would therefore be an additional diagnostic asset. Attempts to accomplish this have been made by various investigators. Unfortunately, the fact that the physical and the chemical properties of vitamin D are not well defined renders difficult its determination by such methods. The biologic test, in which the curative effect of the blood serum on rachitic rats is determined, remains, therefore, the only way practicable at present to determine its vitamin D content.

Hess, Light, Frey and Gross,[1] in a study on cows fed irradiated yeast or viosterol, found that the blood of animals receiving excessive amounts of either viosterol or yeast contained 1 unit of vitamin D in 1.5 Gm. of whole blood whereas the blood of those receiving moderate doses of yeast contained but 1 unit in 2.5 Gm. They stated, furthermore, that the blood plasma contained considerably more vitamin D than the corpuscles.

As a result of a biologic assay of the blood and the feces of infants receiving various antirachitic substances, Hess, Weinstock and Gross[2] stated that "the relatively high potency of, for example, irradiated milk as compared to viosterol, could not be accounted for by the relative amounts of antirachitic factor in the blood. When protective doses

From the Children's Hospital Research Foundation and the Department of Pediatrics, University of Cincinnati.

1. Hess, A. F.; Light, R. F.; Frey, C. M., and Gross, J.: Study of Milk, Blood and Excreta of Cows Fed Moderate and Excessive Amounts of Irradiated Yeast or Ergosterol, J. Biol. Chem. **97**:369-377 (Aug.) 1932.

2. Hess, A. F.; Weinstock, M., and Gross, J.: Biologic Assay of Blood and Feces of Infants Receiving Various Antirachitics, Proc. Soc. Exper. Biol. & Med. **30**:1357-1358 (June) 1933.

were given, notwithstanding the fact that the clinical effect was about the same, a definitely larger number of units was found in the blood of the infants which had received viosterol. Evidently antirachitic effect clinically does not parallel the antirachitic content of the blood as tested on rats."

Coppens and Metz [3] studied the distribution of vitamin D in animals after peroral administration of viosterol and found a certain amount of it in the venous blood in dogs.

Russell, Taylor and Wilcox [4] investigated the distribution of the antirachitic factor from cod liver oil and from viosterol in certain tissues of the chicken. They found that in the blood the factor was contained entirely in the plasma and considered that the solid elements were not involved in its transport. The blood of a group of cockerels, 21 weeks old, each of which had received a diet to which had been added 1 per cent of cod liver oil, contained essentially the same concentration of the antirachitic factor as that of cockerels which had received a diet containing an amount of viosterol equivalent to 24 per cent of cod liver oil.

In a study of the vitamin D content of the blood and the milk of cows fed irradiated yeast, Light, Wilson and Frey [5] examined the blood plasma at hourly intervals for four hours after feeding the animals irradiated yeast. Their results indicate that the absorption of vitamin D in the blood begins between one and two hours after it is ingested. The level of the vitamin D in the blood continues to decline in the first hour after the feeding. From the second to the fourth hour it remains constant.

From these few studies it can be seen that knowledge of the vitamin D content of the blood is still limited and, as Light, Wilson and Frey [5] stated, much work must be undertaken in this field. How little the determination of this content has been applied to clinical studies may be gathered from the fact that no data on the normal vitamin D content of the blood serum in children or adults are yet available.

In view of this situation, further study concerning the usefulness of the biologic method in estimating the vitamin D content of normal and pathologic human blood serums appears to be indicated. Immedi-

3. Coppens, P. A., and Metz, G. A.: Untersuchungen über die Verteilung des bestrahlten Ergosterins (D-Vitamins) im Tierorganismus nach Verabreichung per os, Arch. néerl. de physiol. **18**:407-415, 1933.

4. Russell, W. C.; Taylor, M. W., and Wilcox, D. E.: Fate of the Antirachitic Factor in the Chicken: The Effective Levels and the Distribution of the Factor from Cod Liver Oil and from Irradiated Ergosterol in Certain Tissues of the Chicken, J. Biol. Chem. **107**:735-746 (Dec.) 1934.

5. Light, R. F.; Wilson, L. T., and Frey, C. N.: Vitamin D in Blood and Milk of Cows Fed Irradiated Yeast, J. Nutrition **8**:105-111 (July) 1934.

ately, several questions arise concerning the influence of such factors as the food ingested, starvation, fever, etc., on the vitamin D level of the serum. Since these questions can best be answered by animal experiments, preliminary studies were made on rabbits to elaborate the method. This report presents the result of these experiments, together with a number of estimations of the vitamin D content in normal human serums.

METHOD

The amount of serum required to produce 2 + healing in a rat, prepared in the way to be described later, is considered to contain 1 rat unit.[6]

The rats used were raised on the standard Steenbock diet. After the young had reached a weight of 50 Gm. they were placed three to a cage and given the rickets-producing Steenbock and Black diet, no. 2965, for three weeks.[7] This diet consists of: yellow corn, 76 per cent; wheat gluten, 30 per cent; calcium carbonate, 3 per cent and sodium chloride, 1 per cent. In the beginning the development of rickets was tested by roentgen examination; but since there was no failure in its production as long as the uniform Steenbock and Black diet was given, roentgen examination was later omitted. At the end of the third week the rats were ready for the test. Blood serum in increasing amounts was now fed to three rats, which were kept on the basic Steenbock and Black diet. The aim was to obtain insufficient healing in the first rat, 2 + healing in the second and more than 2 + healing in the third. Often, of course, such results could not be obtained at the first attempt, since the vitamin D level differed from the expected value, and other rats had to be given larger or smaller amounts in order to establish the curative dose.

Since there was much variation in the vitamin D content of different serums, various methods of administration had to be used. For example, only from 0.05 to 0.15 cc. of the serum of a rabbit whose vitamin D level had been raised by huge doses of viosterol was required to cure a rachitic rat. Such small amounts were administered by 0.05 cc. pipets. As a rule, each of the rachitic rats was given a daily dose of 0.05 cc. of blood serum for one, two or three days, respectively. On the other hand, in the blood serum of untreated animals or human beings the vitamin D level is much lower, and therefore larger amounts of serum, i.e., several cubic centimeters, had to be given. The serum was mixed thoroughly with the rickets-producing food. This mixture was fed to the animals during the first eight days of the experiment. It was necessary, of course, to keep each rat in a separate cage during the curative period.

As stated, each value was obtained by testing the serum on from three to six rats. The remainder of the serum was kept in the refrigerator so that if in the assay one value was found to be disproportionate to the amount of serum given, the assay could be repeated on three other rats. This number of rats may be considered small for an exact biologic test,[8] but the amount of human serum that is

6. One rat unit of vitamin D corresponds to 2.7 U. S. P. XI units.

7. Steenbock, H., and Black, A.: Fat-Soluble Vitamins: Induction of Growth-Promoting and Calcifying Properties in Fats and Their Unsaponifiable Constituents by Exposure to Light, J. Biol. Chem. **64**:263-298 (June) 1925.

8. Bills, C. E.; Honeywell, E. M.; Wirick, A. M., and Nussmeier, M.: Critique of the Line Test for Vitamin D, J. Biol. Chem. **90**:619-636 (Feb.) 1931.

available for diagnostic purposes is limited. Then, too, in the experiments on rabbits I was satisfied to ascertain the general trend of the vitamin D level. The changes of the level were marked in individual rabbits, and the variability of absorption was far beyond the limit of error of the method of estimation. Further accuracy in the determination of the value in a single serum would not have influenced the general trend of the vitamin D curve to any great extent.

EXPERIMENTS

1. *Changes of the Vitamin D Level of the Blood Serum in Rabbits After Administration of 0.1 Cc. of Viosterol.*[9]—An experiment was made to determine the increase and consequent decrease of the vitamin D level in the blood serum after administration of large amounts of viosterol.

White New Zealand and brown and gray Havana rabbits, weighing from 2,500 to 3,000 Gm. and fed on hay and oats, were used. Preliminary tests were done on normal rabbits from the experimental group to determine the vitamin D level of the blood serum before administration of viosterol. The amount of serum required to produce 2+ healing in a rachitic rat was found to be 6 cc. Thus the blood serum of a normal rabbit on the diet mentioned contains 17 rat units (46 U. S. P. units) per hundred cubic centimeters.[10]

On the first day of the experiment the animals were each given 0.1 cc. of viosterol (100,000 U. S. P. units) by pipet. At intervals they were bled. The blood was allowed to clot and then was centrifugated. The serum was pipetted off and fed in varying amounts to the rachitic rats in the manner previously described. Estimations of the increase of the vitamin D level in the serum were made after one hour, two hours, six hours, twenty-four hours, forty-eight hours, three days, four days, five days, eight days, etc., until, after three weeks, the vitamin D level had returned to normal. Tables 1 and 2 show the results of two typical experiments.

Deviations from the usual increase were sometimes encountered, although the procedure was alike in all the experiments. In table 3 are shown the complete results of an experiment in which some of the values are 100 per cent below the average. Whether this low curve was caused by lessened absorption or increased excretion of vitamin D was not evident from the experiment.

In spite of these variations, a general trend may be seen in the curves. As early as six hours after the administration of viosterol a marked increase of the vitamin D content in the blood serum could be noted. Fourteen determinations were made twenty-four hours after the administration of 0.1 cc. of viosterol (100,000 U. S. P. units). Ten samples of serum showed a vitamin D value of 1,000 rat units

9. Mead Johnson & Co. furnished the viosterol used in this study. The concentration was 1,000,000 U. S. P. units of vitamin D to 1 cc. of viosterol.

10. Decimal fractions of units are omitted, as they were of little significance.

TABLE 1.—*Experiment 1: Typical Results*

Rabbit 1,355: female, New Zealand, white. Food: Purina Chow.

Date	Rat	Weight of Rabbit, Gm.	Amount of Serum Given to Rat, Cc.	Line Test	Vitamin D Content of Rat's Serum, per 100 Cc.	
					Rat Units	U.S.P. Units
8/27/34	..	2,130	Received 0.1 cc. of viosterol (100,000 U.S.P. units)			
8/28/34	..	2,280	24 hours later:			
	18	.....	0.025	+		
	13	.....	0.05	+		
	20	.....	0.1	++		
					1,000	2,700
8/31/34	..	2,265	4 days later:			
	12	.....	0.025	+/++		
	16	.....	0.05	0/+		
	17	.....	0.1	+++		
					1,000	2,700
9/ 6/34	..	2,435	10 days later:			
	24	.....	0.025	0		
	25	.....	0.05	0		
	26	.....	0.1	+		
	38	.....	0.2	++		
					500	1,350
9/11/34	..	2,430	15 days later:			
	15	.....	0.05	0		
	19	.....	0.1	0		
	14	.....	0.2	+		
	39	.....	0.3	+++		
					330	891
9/17/34	..	2,545	21 days later:			
	32	.....	0.3	0		
	33	.....	0.4	0		
	34	.....	0.5	0		
	60	.....	0.7	++		
	61	.....	1.0	+++		
					140	378
9/22/34	..	.....	26 days later:			
	35	.....	0.4	0		
	36	.....	0.5	0		
	37	.....	0.6	0		
	59	.....	1.0	+		
					<100	<270
10/ 8/34	..	2,850	42 days later:			
	64	.....	5.0	+		
					<20	<54

TABLE 2.—*Experiment 1: Typical Results*

Rabbit 1,386: male, black and white. Food: oats, hay, greens.

Date	Rat	Weight of Rabbit, Gm.	Amount of Serum Given to Rat, Cc.	Line Test	Vitamin D Content of Rat's Serum, per 100 Cc.	
					Rat Units	U.S.P. Units
9/26/34	..	2,830	Received 0.1 cc. of viosterol (100,000 U.S.P. units)			
			6 hours later:			
	62	.....	0.05	0		
	63	.....	0.1	+		
	41	.....	0.2	+++		
	42	.....	0.3	++/+++		
	43	.....	0.4	+++		
					500	1,350
9/27/34	..	2,890	24 hours later:			
	53	.....	0.025	0		
	54	.....	0.05	+		
	55	.....	0.1	+++		
					1,000	2,700
9/28/34	..	2,715	48 hours later:			
	44	.....	0.025	0		
	45	.....	0.05	+		
	46	.....	0.1	+++		
					1,000	2,700
10/ 2/34	..	2,560	6 days later:			
	56	.....	0.05	0		
	57	.....	0.1	+		
	58	.....	0.2	++/+++		
					500	1,350
10/ 6/34	..	2,720	10 days later:			
	65	.....	0.05	0		
	66	.....	0.1	0		
	67	.....	0.2	+		
	88	.....	0.25	++		
	89	.....	0.3	++		
					400	1,080

(2,700 U. S. P. units) per hundred cubic centimeters; two, a value of 660 rat units (1,782 U. S. P. units); one, a value of 1,330 rat units (3,591 U. S. P. units), and one, a value of 500 rat units (1,350 U. S. P. units). After forty-eight hours six determinations were made, five giving a value of 1,000 rat units (2,700 U. S. P. units) and one a value of 500 rat units (1,350 U. S. P. units). One determination after three days showed a value of 500 rat units (1,350 U. S. P. units). After

TABLE 3.—*Experiment 1: Values Lower Than the Average*

Rabbit 1,785: male, Havana, silver gray. Food: oats, hay, greens.

Date	Rat	Weight of Rabbit, Gm.	Amount of Serum Given to Rat, Cc.	Line Test	Vitamin D Content of Rat's Serum, per 100 Cc.	
					Rat Units	U.S.P. Units
4/ 9/35	...	2,605	Received 0.1 cc. of viosterol (100,000 U.S.P. units)			
4/10/35	...	2,615	24 hours later:			
	427	.....	0.025	0		
	429	.....	0.025	0		
	430	.....	0.05	0		
	431	.....	0.075	0		
	428	.....	0.1	+		
	453	.....	0.15	0/+		
	454	.....	0.2	++		
					500	1,350
4/12/35	...	2,530	3 days later:			
	435	.....	0.025	0		
	436	.....	0.05	0		
	437	.....	0.075	+		
	432	.....	0.075	+		
	433	.....	0.1	+		
	434	.....	0.15	+/++		
	456	.....	0.2	++/+++		
					500	1,350
4/13/35	...	2,550	4 days later:			
	439	.....	0.075	0		
	438	.....	0.1	+		
	440	.....	0.15	+/++		
	458	.....	0.2	++		
					500	1,350
4/15/35	...	2,520	6 days later:			
	441	.....	0.1	0		
	442	.....	0.2	+		
	443	.....	0.3	++		
	444	.....	0.3	++		
	445	.....	0.4	++/+++		
	446	.....	0.5	++		
					330	891
4/25/35	...	.....	16 days later:			
	462	.....	0.7	0		
	463	.....	1.0	0		
	479	.....	2.0	+		
					<50	<135

four days five determinations resulted in four values of 1,000 rat units (2,700 U. S. P. units) and one of 500 rat units (1,350 U. S. P. units). After five days all determinations gave a value of less than 1,000 rat units (2,700 U. S. P. units), and a definite tendency to return to normal could be recognized. Finally, forty-two days after the administration of 0.1 cc. of viosterol (100,000 U. S. P. units), the average normal range was reached.

Chart 1 shows a compilation of all the values obtained for the fourteen rabbits used. Each rabbit for which four estimations or more were obtained is represented by a special symbol. If less than four estimations were made, the values are represented by dots.

From this chart it can be seen that some of the values differ widely from the average, as is to be expected in a biologic experiment tested by a biologic method. The deviations should be emphasized to point out the necessity for caution in the interpretation of experiments performed for the purpose of examining factors that might influence the vitamin D level. Experiments 4, 5 and 6 were of that type. It should be noted, however, that the values found for rabbits 1785 and 1386-2 form curves that run consistently higher or lower than the aver-

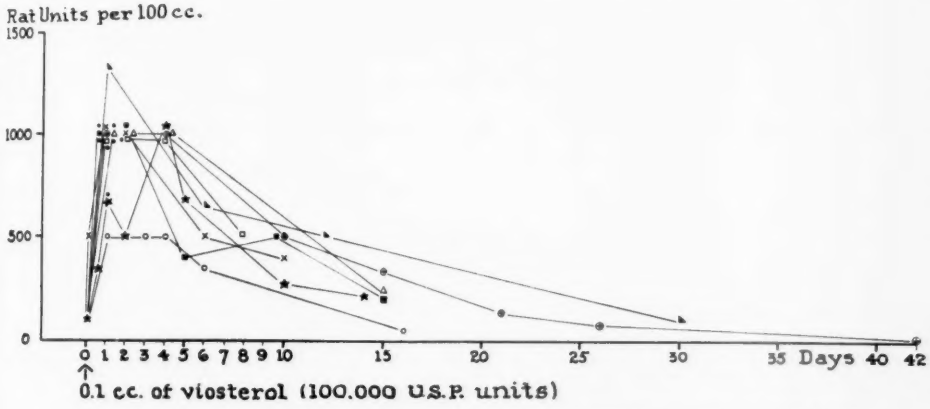

Chart 1.—A graph showing the elevation of the vitamin D level in the blood serum of rabbits after the peroral administration of 0.1 cc. of viosterol (100,000 U. S. P. units). Each symbol represents a rabbit, as follows: rabbit 1355, circle with cross; rabbit 1386, cross; rabbit 1786, hollow triangle; rabbit 1788, star; rabbit 1477, solid square; rabbit 1386-2, solid triangle; rabbit 1785, hollow circle; rabbit 1650-2, hollow square.

age, thus suggesting that the deviations are caused by different reactions of the individual rabbit rather than by inaccuracy of the method.

2. *Comparison of the Direct and Indirect Methods of Determining Changes in the Vitamin D Content in the Living Organism.*—Determinations of the inorganic phosphorus, the calcium, the phosphatemic curve [10a] and the phosphatase content of the blood serum are employed in estimating the changes which occur with varying supplies of vitamin D. In this experiment these indirect methods are compared with the direct (biologic) estimation of the vitamin D content in the blood serum

10*a*. Warkany, J.: Die phosphatämische Kurve des normalen und des rachitischen Organismus: I and II, Ztschr. f. Kinderh. **46**:1-12 and 716-722, 1928.

in the normal organism after ingestion of a large but not toxic dose of viosterol.

About 40 cc. of blood was obtained from a rabbit, and the serum was separated from the corpuscles. The inorganic phosphorus, calcium, phosphatase and vitamin D levels were determined. Eleven days later the phosphatemic curve was determined by the same rabbit. The results are shown in table 4.

TABLE 4.—*Experiment 2*

Rabbit 1,789: female, New Zealand, white. Food: oats, hay.

5/16/35	Weight: 2,380 Gm.	
	Blood serum: Inorganic phosphorus content	5.5 mg. per 100 cc.
	Calcium content	15.2 mg. per 100 cc.
	Phosphatase content	2.9 units per 100 cc.
	Vitamin D level: Less than 20 rat units (54 U.S.P. units) per 100 cc.	
	Rat	4 cc. of serum administered. Line test: 0
	Rat	5 cc. of serum administered. Line test: 0
5/27/35	Weight: 2,460 Gm.	
	Phosphatemic curve:	
	Fasting: inorganic phosphorus	7.1 mg. per 100 cc
	Peroral administration of 1.5 Gm. of di-sodium hydrogen phosphate ($Na_2HPO_4.12H_2O$)	
	2 hours later: inorganic phosphorus content	9.1 mg. per 100 cc.
	P increase = 2 mg. per 100 cc.	

TABLE 5.—*Experiment 2*

Rabbit 1,789

7/17/35	Weight: 2,964 Gm. Received 0.1 cc. of viosterol (100,000 U.S.P. units)		
7/18/35	Weight: 2,947 Gm.		
	Blood serum: Inorganic phosphorus content	5.8 mg. per 100 cc.	
	Calcium content	15.9 mg. per 100 cc.	
	Phosphatase content	3.0 units per 100 cc.	
	Vitamin D level: 1,000 rat units (2,700 U.S.P. units) per 100 cc.		
	Rat	Amount of Serum Given, Cc.	Line Test
	604	0.05	+
	605	0.10	+++
	606	0.15	+++
7/19/35	Phosphatemic curve		
	Fasting: Inorganic phosphorus	6.3 mg. per 100 cc.	
	Peroral administration of 1.5 Gm. of di-sodium hydrogen phosphate ($Na_2HPO_4.12H_2O$)		
	2 hours later: Inorganic phosphorus	9.2 mg. per 100 cc.	
	P increase = 2.9 mg. per 100 cc.		

Two months after the first blood was taken the rabbit received 0.1 cc. of viosterol. Twenty-four hours later the inorganic phosphorus, calcium, phosphatase and vitamin D levels of the serum were again determined. The phosphatemic curve was calculated on the following day. The findings are given in table 5.

The values for blood phosphorus, calcium and phosphatase and the phosphatemic curve did not undergo a significant change after the administration of 0.1 cc. of viosterol (100,000 U. S. P. units), while the vitamin D content increased at least 500 times. Thus direct estima-

tion was found to be decidedly the most sensitive method for the demonstration of changes in the vitamin D content of the blood serum in the normal organism.

3. *Vitamin D Level after Administration of 1 Cc. of Viosterol (1,000,000 U. S. P. Units).*—An experiment was made to determine the effect on the blood serum of rabbits of the administration of 1 cc. of viosterol.

TABLE 6.—*Experiment 3*

Rabbit 1,077: New Zealand, white. Food: Purina Chow.

Date	Rat	Weight of Rabbit, Gm.	Amount of Serum Given to Rat, Cc.	Line Test	Vitamin D Content of Rat's Serum, per 100 Cc. Rat Units	Vitamin D Content of Rat's Serum, per 100 Cc. U.S.P. Units
4/30/34	...	2,700	Inorganic phosphorus content, 6.6 mg. per 100 cc. Serum calcium content, 13.2 mg. per 100 cc.			
	114	.....	2.0	0		
	115	.....	2.0	0		
					<50	<135
5/ 9/34	...	.....	Received 1 cc. of viosterol (1,000,000 U.S.P. units)			
			1 hour later:			
	118	.....	0.5	0		
	119	.....	1.0	0		
					<100	<270
			6 hours later: Inorganic serum phosphorus content, 5.8 mg. per 100 cc. Serum calcium content, 13.2 mg. per 100 cc.			
			0.01	0		
	136	.....	0.02	+		
	137	.....	0.05	+++/++++		
	138	.....	0.08	+++/++++		
	100	.....	0.1	+++		
	101	.....	0.2	+++		
					2,000	5,400
5/10/34	...	2,185	24 hours later: Inorganic serum phosphorus content, 8.0 mg. per 100 cc. Serum calcium content, 12.8 mg. per 100 cc.			
	132	.....	0.005	0		
	133	.....	0.01	++		
	106	.....	0.02	+++		
	107	.....	0.05	+++		
					10,000	27,000
5/11/34	...	1,950	48 hours later: Inorganic serum phosphorus content, 11.7 mg. per 100 cc. Serum calcium content, 12.1 mg. per 100 cc.			
	8	.....	0.0025	0		
	134	.....	0.005	++		
	135	.....	0.01	++/+++		
	103	.....	0.02	+++		
	104	.....	0.05	+++		
					20,000	27,000
5/12/34		Dead				

One cubic centimeter of viosterol (1,000,000 U. S. P. units), that is, ten times the dose given in the experiments reported so far, is a toxic dose for a rabbit and often causes death. Two cubic centimeters of the rabbit's blood serum did not produce healing before the viosterol was given (table 6). Six hours after the administration of 1 cc. of viosterol as little as 0.05 cc. of blood serum produced from + 3 to 4 + healing in the test rat (a vitamin D content of 2,000 rat units, or 5,400 U. S. P. units, per hundred cubic centimeters of serum). After twenty-four hours there was a value of 10,000 rat units (27,000 U. S. P. units), and

forty-eight hours later a value of 20,000 rat units (54,000 U. S. P. units). The next day the rabbit was found dead. The inorganic phosphorus and the calcium content were determined for each blood sample (chart 2). The inorganic phosphorus content definitely increased after twenty-four and forty-eight hours, while the calcium content decreased slightly. It is to be noted that six hours after the administration of viosterol the serum phosphorus content had not increased. The vitamin D level of the blood serum, however, had already reached 2,000 rat units (5,400 U. S. P. units) per hundred cubic centimeters, thus preceding the chemical changes.

4. *Influence of Ether Anesthesia on the Vitamin D Level.*—As soon as the course of the vitamin D level in the blood serum had been established after the ingestion of viosterol, an attempt was made to find out

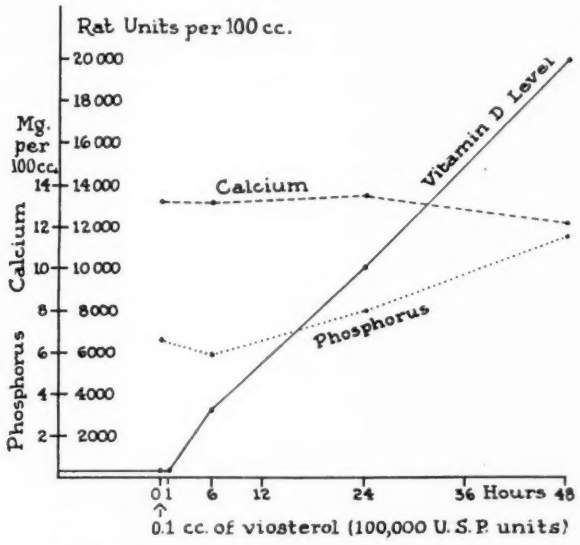

Chart 2.—A graph showing the behavior of the vitamin D level, the calcium content and the inorganic phosphorus content of the blood serum of a rabbit after the peroral administration of 1 cc. of viosterol (1,000,000 U. S. P. units).

whether ether anesthesia could influence a high level. This knowledge seemed of interest since some experiments were planned on anesthetized animals and the possible influence of the anesthesia had to be taken into consideration. The experiments were conducted as follows:

A rabbit was bled after peroral administration of viosterol. Immediately after the blood was procured the animal was anesthetized with ether for twenty minutes and then bled again. The two samples of blood serum obtained were compared with respect to their vitamin D content. Table 7 shows that a vitamin D level of 1,000 rat units (2,700 U. S. P. units) was uninfluenced by anesthesia maintained for twenty minutes. In two other experiments the same fact was shown for a vitamin D level of 500 rat units (1,350 U. S. P. units). Table 8 shows the results of one of these experiments.

5. *Influence of Fever.*—Experiments were made to determine the effect of fever on a high vitamin D level of the blood and on the rate of absorption of vitamin D from the intestinal tract.

(*a*) In the experiments on the effect of fever, the rabbit was given 0.1 cc. of viosterol and twenty-four hours later was bled. The vitamin D level was found to be 1,000 rat units (2,700 U. S. P. units) per hundred cubic centimeters. At that time the temperature was normal. Bacillus coli vaccine was now administered intravenously and brought about an increase in temperature of approximately 4 F.

TABLE 7.—*Experiment 4: Influence of Ether Anesthesia on the Vitamin D Level*
Rabbit 1,786-2: female, Havana, brown. Food: hay and oats.

Date	Rat	Weight of Rabbit, Gm.	Amount of Serum Given to Rat, Cc.	Line Test	Vitamin D Content of Rat's Serum, per 100 Cc. Rat Units	U.S.P. Units
8/12/35	...	2,780	Received 0.1 cc. of viosterol (100,000 U.S.P. units)			
8/13/35	...	2,740	24 hours later:			
	663	.....	0.05	+		
	664	.....	0.1	++		
	665	.....	0.15	++		
					1,000	2,700
			Ether anesthesia for 20 minutes			
	666	.....	0.05	+		
	667	.....	0.1	++		
	668	.....	0.15	+++		
					1,000	2,700

TABLE 8.—*Experiment 4: Influence of Ether Anesthesia on Vitamin D Level*
Rabbit 1,650-2: female, New Zealand, white. Food: hay and oats

Date	Rat	Weight of Rabbit, Gm.	Amount of Serum Given to Rat, Cc.	Line Test	Vitamin D Content of Rat's Serum, per 100 Cc. Rat Units	U.S.P. Units
6/13/35	...	2,960	Received 0.1 cc. of viosterol (100,000 U.S.P. units)			
6/21/35	...	3,005	8 days later:			
	572	.....	0.2	+/++		
	573	.....	0.2	++		
	574	.....	0.3	+++/++++		
					500	1,350
			Ether anesthesia for 20 minutes			
	575	.....	0.15	+		
	576	.....	0.2	++		
	577	.....	0.3	+++		
					500	1,350

Twenty-four hours later, i. e., forty-eight hours after the animal had received viosterol, it was bled again and the vitamin D level was found to be 1,000 rat units (2,700 U. S. P. units) or a level that would be expected in the same rabbit without fever.

It may be concluded from this experiment that a short period of elevated temperature does not influence a high vitamin D level to a marked degree.

(*b*) The next question was whether absorption of vitamin D during fever differs from absorption in a normal organism. A rabbit received two injections

of B. coli vaccine. After the temperature had risen the animal was given 0.1 cc. of viosterol (100,000 U. S. P. units). Then two larger doses of B. coli vaccine were given, keeping the temperature elevated for twenty-four hours. After that interval

TABLE 9.—*Experiment 5: Influence of Fever on Vitamin D Level*

Rabbit 1,790-2: female, New Zealand, white. Food: hay and oats.

Date	Rat	Weight of Rabbit, Gm.	Amount of Serum Given to Rat, Cc.	Line Test	Vitamin D Content of Rat's Serum, per 100 Cc.	
					Rat Units	U.S.P. Units
8/ 9/35	...	2,615	Received 0.1 cc. of viosterol (100,000 U.S.P. units)			
8/10/35	...	2,580	24 hours later:			
	654	.....	0.05	0		
	655	.....	0.1	++		
	656	.....	0.15	+++		
					1,000	2,700
			11 a.m., temperature 102.4 F.			
			Received 0.3 cc. of B. coli vaccine intravenously			
			6 p.m., temperature 105.5 F.			
			9 p.m., temperature 106.2 F.			
			11 p.m., temperature 106.2 F.			
8/11/35	...	2,315	10 a.m., temperature 103 F.			
			48 hours later:			
	657	.....	0.05	+		
	658	.....	0.1	++		
	659	.....	0.15	++		
					1,000	2,700

TABLE 10.—*Experiment 5: Absorption of Vitamin D During Fever*

Rabbit 1,478: female, New Zealand, white. Food: hay, oats.

Date	Hour	Weight, Gm.	Temperature, F.	Amount of B. Coli Vaccine Received, Cc.
10/31/34	.....	2,112	103.4	
11/ 2/34	10:35 a.m.	2,350	102.9	
	11:15	.....	103.5	0.25
	12:00	.....	104.2	0.3
	Received 0.1 cc. of viosterol (100,000 U.S.P. units)			
	1:30 p.m.	.....	104.4	
	2:15	.....	104.8	0.5
				1.5
	6:00	.....	104.2	
	12:00	.....	104.4	
11/ 3/34	10:00 a.m.	.....	105.0	
	12:00	.....	105.2	

Rat	Amount of Serum Given to Rat, Cc.	Line Test	Vitamin D Content of Rat's Serum, per 100 Cc.	
			Rat Units	U.S.P. Units
	24 hours later:			
130	0.025	0		
131	0.05	0		
132	0.075	0		
117	0.1	+++		
116	0.15	+++		
			1,000	2,700

the rabbit was bled, and the vitamin D content of the blood serum was determined and compared with that expected from the normal curve (1,000 rat units, or 2,700 U. S. P. units). As can be seen from table 10, the value during fever was identical with the corresponding value of the normal curve.

Elevation of temperature did not change the rate of absorption of vitamin D from the intestinal tract.

6. *Influence of Starvation.*—That starvation causes hyperlipemia is a well known fact. Also, it has been shown repeatedly that the cholesterol level rises during the early days of fasting.[11] Therefore, a study of the effect of viosterol during starvation seemed of interest.

TABLE 11.—*Experiment 6: Influence of Starvation on the Vitamin D Level*
Rabbit 1,868: female, New Zealand, white. Food: hay and oats.

Date	Rat	Weight of Rabbit, Gm.	Amount of Serum Given to Rat, Cc.	Line Test	Vitamin D Content of Rat's Serum, per 100 Cc. Rat Units	U.S.P. Units
8/19/35	...	2,265	Received 0.1 cc. of viosterol (100,000 U.S.P. units) Water only for 48 hours			
8/20/35	...	.....	24 hours later:			
	696	.....	0.05	+		
	697	.....	0.10	++		
	698	.....	0.15	++		
					1,000	2,700
8/21/35	...	2,130	48 hours later:			
	699	.....	0.05	+		
	700	.....	0.10	++/+++		
	701	.....	0.15	++/+++		
					1,000	2,700

TABLE 12.—*Comparison of Feeding by Pipet and Cup*
Rabbit 1,650-3: female, New Zealand, white. Food: oats and hay.

Date	Rat	Weight of Rabbit, Gm.	Amount of Serum Given to Rat, Cc.	Line Test	Vitamin D Content of Rat's Serum, per 100 Cc. Rat Units	U.S.P. Units
8/26/35	...	3,615	Received 0.1 cc. of viosterol (100,000 U.S.P. units)			
8/27/35	...	3,615	24 hours later:			
	729	.....	0.05 (by pipet)	+		
	730	.....	0.1 (by pipet)	+		
	731	.....	0.15 (by pipet)	++		
					660	1,782
			Diluted 1:20, fed from cups:			
	726	.....	1 (= 0.05 cc. of original serum)	0		
	727	.....	2 (= 0.1 cc. of original serum)	+		
	728	.....	3 (= 0.15 cc. of original serum)	++		
					660	1,782

A rabbit which had received 0.1 cc. of viosterol (100,000 U. S. P. units) was starved for from twenty-four to forty-eight hours, water only being given. The blood serum was examined, and the results were compared to the normal curve to determine whether or not starvation influences the vitamin D content. As can be seen from table 11, the vitamin D level after twenty-four and forty-eight hours was 1,000 rat units (2,700 U. S. P. units), the same as that in animals fed in the usual way.

11. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry: Interpretations, Baltimore, Williams & Wilkins Company, 1932, p. 243.

ESTIMATIONS OF THE VITAMIN D CONTENT OF HUMAN SERUM

In applying this method to clinical studies the fact that the normal level of vitamin D in the serum of the human subject is lower than the artificial range in animals must be considered. Much larger amounts

TABLE 13.—*Estimations of the Vitamin D Content of Human Blood Serum*

	Age of Subject, Years	Month	Content per 100 Cc.	
			Rat Units	U.S.P. Units
P. B.	7	December	40	108
E. L.	7	December	25	67
P. M.	7	December	50	135
G. L.	7	December	33	89
C. B.	7	December	33	89
B. A.	7	December	40	108
L. A.	8	October	40	108
		December	33	89
A. C.	8	December	40	108
J. C.	8	December	33	89
V. C.	8	December	50	135
A. N.	8	December	33	89
W. Sm.	9	January	40	108
W. S.	9½	June	28	76
	10	October	40	108
S. B.	10	June	28	76
	10	October	33	89
D. L.	10	October	40	108
J. P.	10	October	25	67
E. F.	10	October	40	108
D. W.	10	December	33	89
	10	January	33	89
G. W.	11	October	40	108
J. C.	11	October	50	135
W. C.	11	October	50	135
J. G.	11	November	40	108
H.	11	December	30	81
O. R.	11	December	25	67
H. G.	11	December	40	108
B. A.	12	December	33	89
G. C.	12	December	33	89
W. W.	12	May	40	108
J. A.	14	November	33	89
R. G.	15	September	50	135
E. B.	21	August	33	89
J. P.	25	September	50	135
J. W.	32	May	50	135
		August	33	89
		September	40	108
		October	33	89
		December	40	108
	33	March	33	89
		May	17	46
		September	40	108
		November	33	89
		January	33	89
		January	40	108
E. B.	39	October	33	89

of the blood serum of normal children or adults must be given to cure the rickets of test rats.

Since several cubic centimeters of blood serum could not be given by pipet, the serum was mixed thoroughly with food and fed to the rats over a period of eight days. To test whether the two methods of administration are comparable, the blood serum of a rabbit that had previously received viosterol was fed in amounts

of 0.05, 0.1 and 0.15 cc. to different rats, and a vitamin D level of 660 rat units (1,782 U. S. P. units) was established. Some of the same serum was diluted with water (1:20) and 1 cc. (corresponding to 0.05 cc. of the original serum), 2 cc. (corresponding to 0.1 cc.) and 3 cc. (corresponding to 0.15 cc.) were mixed with rickets-producing food and fed to rats that were kept in separate cages. The result was found to be the same as that of feeding by pipet (table 12).

Therefore, the method of adding the serum to food, used in the estimations of the vitamin D content of human serums, can be compared with the method of feeding by pipet.

In table 13 the results of forty-eight estimations of the vitamin D content in the blood serum are tabulated according to the age of the subject, independent of sex and race. The serum was given in increasing amounts, each being 0.5 cc. larger than the last. No attempt was made to reach an accuracy beyond the 0.5 cc. interval. From 2 to 6 cc. of blood serum was required to cure rachitic rats. That is, values of from 17 to 50 rat units (from 46 to 135 U. S. P. units) per hundred cubic centimeters of serum were found for the forty-eight blood samples. The average value was 36.7 rat units (99.1 U. S. P. units). From table 13 no influence of age can be deduced. Studies to determine the influence of seasonal changes and pigmentation of the skin are in progress.

COMMENT

Changes of the vitamin D level of the blood serum after oral ingestion of viosterol have been demonstrated in the experiments reported. Variations in the reactions of individual animals have been noted, but a general trend of increase and decrease of the vitamin D level can be demonstrated. In agreement with the findings of Light, Wilson and Frey,[5] it has been shown that the ingested vitamin D appears in the blood stream after a few hours. After the administration of 0.1 cc. of viosterol (100,000 U. S. P. units) the peak of the curve is generally reached in twenty-four hours. The values are then maintained until about the fourth day. Later a slow decrease of the vitamin D content is noted, until after from four to six weeks the elevation is no longer manifest. The period between the first and the fourth day, the time of a constant high level, is recommended for the examination of factors that might influence the vitamin D level (experiments 4, 5 and 6).

Since the vitamin D levels in experimental animals are far beyond the physiologic range, generalizations must be made with care. Although fever, ether anesthesia and starvation did not influence a vitamin D level of 1,000 rat units (2,700 U. S. P. units) per hundred cubic centimeters, it is conceivable that the physiologic level of from 17 to 50 rat units (from 46 to 135 U. S. P. units) can be altered by such factors. A decrease or increase of 20 rat units (54 U. S. P. units), which would amount to a 50 per cent change under physiologic conditions, is negligible and within the limit of error in the animal experiments reported.

These experiments are to be considered merely a preliminary attempt to demonstrate the dynamic changes of the vitamin D content within the living organism. The few estimations for children and adults indicate the normal range of this constituent in the blood serum. The influence of age, diet, pigmentation of the skin and season may account for some of the variation. Only a large number of estimations in which these factors are considered will lead to standard values.

The diagnosis of vitamin D intoxication from overdosage should be supported by direct estimation of the vitamin D level in the blood. This is important since the clinical symptoms of vitamin D intoxication (vomiting, cystitis, pyelitis and nephritis) are not pathognomonic and since, as shown in experiment 2, a marked increase of the vitamin D content may occur in the blood when there is no significant change in the blood calcium, blood phosphorus or blood phosphatase level or in the phosphatemic curve.

A lack of vitamin D in the organism, as found in cases of infantile rickets, can be diagnosed clinically and by roentgen examination and can be confirmed by determination of the phosphorus content of the blood. An estimation of the vitamin D content is not required. However, it may be of value in cases in which clinical and roentgenographic findings do not agree with the chemical studies and in those rare cases in which rickets resists vitamin D treatment.

The method of direct estimation may also be applied to studies of the etiology of diseases of the bones to be distinguished from rickets, such as celiac rickets, renal rickets or the various forms of osteoporosis.

SUMMARY

1. After oral administration of 0.1 cc. of viosterol (100,000 U. S. P. units) to rabbits there is an elevation of the vitamin D level within six hours. After twenty-four hours the maximum, generally a level of 1,000 rat units (2,700 U. S. P. units) per hundred cubic centimeters, is reached. This value is maintained for from three to four days. The content then slowly decreases and after from four to six weeks returns to normal.[12]

2. No influence of ether anesthesia, starvation or fever on a high vitamin D level can be demonstrated.

12. After this paper was sent to press, a paper by W. Heymann (Studies on the Mode of Action and Metabolism of Vitamin D, J. Pediat. **8:** 480-488, 1936) appeared. He tested qualitatively the blood serum of rabbits for vitamin D after the administration of 1.6 mg., or 20 cc., of viosterol (200,000 U.S.P. units of vitamin D) and found that from two and one-half to three months is needed to destroy or excrete this amount of vitamin D.

3. Elevation of the vitamin D level after administration of 0.1 cc. of viosterol (100,000 U. S. P. units) occurs without change of the phosphorus, calcium or phosphatase content of the blood or of the phosphatemic curve. For demonstrating changes of the vitamin D content in the normal animal direct estimation seems more sensitive than the chemical methods.

4. After oral administration of 1 cc. of viosterol (1,000,0000 U. S. P. units) values as high as 20,000 rat units (54,000 U. S. P. units) per hundred cubic centimeters of blood serum were found.

5. In forty-eight estimations of the vitamin D content in normal human blood serums, values of from 17 to 50 rat units (from 45.9 to 135 U. S. P. units) per hundred cubic centimeters were found, with an average value of 36.7 rat units (99.09 U. S. P. units).

A STUDY OF THREE HUNDRED AND THIRTY PREMATURE INFANTS

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In the Sloane Hospital for Women, under Dr. William E. Studdiford's direction, a member of the staff of pediatrics was given the responsibility of caring for infants. When, in 1928, the Sloane Hospital for Women joined with other New York hospitals, including the Babies Hospital, in forming the Columbia-Presbyterian Medical Center, closer cooperation between obstetrics and pediatrics was possible. Since that time the department of pediatrics has staffed the nurseries and taken care of the infants within the department of obstetrics.

The purpose of this paper is to give an account of the methods followed and the results obtained in the care of premature infants. The period chosen was exactly five years, extending from Sept. 1, 1929, to Aug. 31, 1934. During this time there were 10,163 consecutive births to mothers in the public wards. Three hundred and thirty, or 3.24 per cent, of the infants weighed 2,500 Gm. or less at birth and on this basis were regarded as premature. Weight was selected as the criterion of prematurity for the following reasons:

Three standards are available for defining and evaluating the degree of prematurity: the period of gestation and the length and the weight of the infant at birth. Of these, the period of gestation has been honored by tradition, notwithstanding the fact that its computation, which depends on the date of last menstruation rather than on real knowledge of the date of conception, is notoriously inaccurate. In figures 1, 2 and 3 the interrelation of the three standards is portrayed for the infants of this series. The correlations between the period of gestation and both the length and the weight of the infant at birth are obviously low; the correlation between the length and the weight is much higher. Even if the estimates of the period of gestation were accurate, the low correlation between the duration of pregnancy and the size of the infant at birth would seem to preclude its practical usefulness as a standard of prematurity, since the problem of medical care is related more closely to size than to fetal age. Because growth in length is more independent of environmental influences than is growth in weight, both

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in intra-uterine and in early extra-uterine life, it is obvious that a linear measurement, such as the body length, constitutes the most reliable gage of maturity, provided that it is accurately obtained. It is my impression that in routine work, unless all the observations are made by one person, the error of measurement of body length is greater than that of body weight; in the series reported on in this paper, a number of observers necessarily took part in obtaining measurements. The technical difficulty of accurately determining body length doubtless is in part responsible for the fact that of the 330 infants selected for this study of prematurity on the basis of body weight, a record of the length at birth was

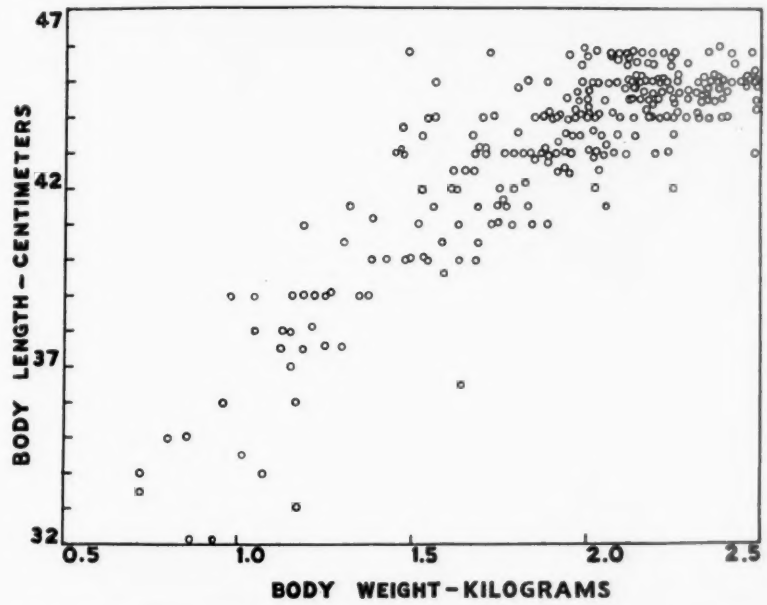

Fig. 1.—Correlation of weight at birth with length of 250 premature infants.

made of only 250. It seems obvious that in a study based on examination of records extending over years, body weight provides the more desirable standard of classification.

CARE AND TREATMENT

When the new hospital was opened, a separate nursery was provided in which premature infants could be segregated. This division consists of a large room, containing incubators and cribs, and a small adjoining wing, with facilities for giving baths and treatments. The temperature of the room is not under automatic control but is kept at approximately 80 F. No attempt is made to regulate the humidity of the room. The

incubators are all of the Morgenthaler type and have individual heating and humidifying equipment. The temperature within the incubators is maintained between 85 and 90 F. The humidity is self regulating, so that the higher the temperature in the incubator and the lower the humidity of the outside air, the more rapidly does evaporation take place from the moistening pad in the lower chamber of the incubator. When the incubator is in operation, the humidity of the upper chamber is

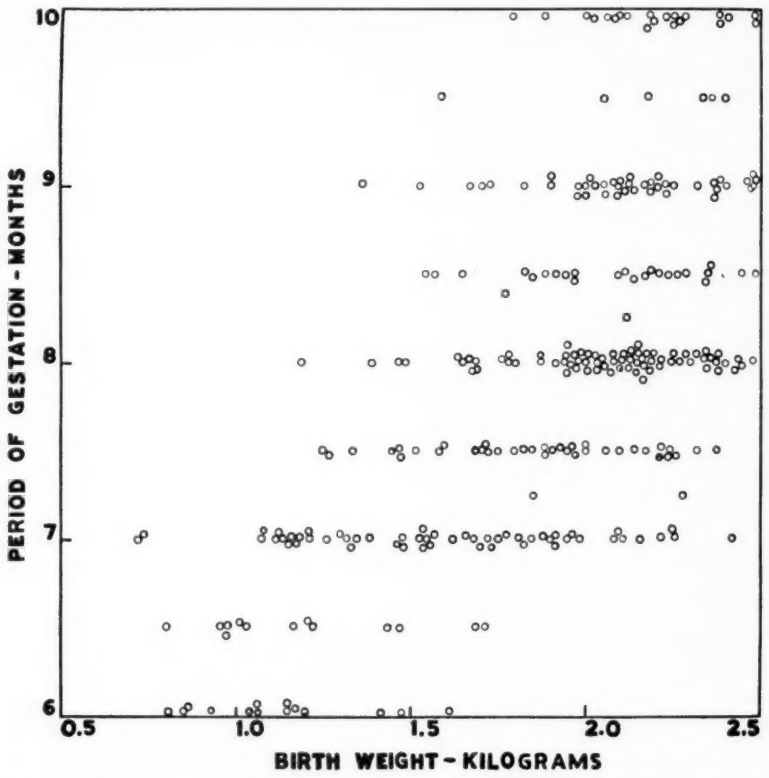

Fig. 2.—Correlation of weight at birth of 290 premature infants with period of gestation.

always maintained between 55 and 60 per cent. All persons entering the nursery for premature infants, except the nurses on duty, wear unsterile gowns and masks covering the nose and mouth.

Immediately after the infant has been born in the delivery room, he is wrapped in a sterile heated blanket and is carried as quickly as possible down a flight of stairs to the nursery. He is weighed, and his temperature is taken rectally. If he weighs less than 2,050 Gm. or if he weighs more than 2,050 Gm. but has a temperature of less than

96 F., he is dressed at once, without being bathed, and is put immediately into an incubator. If the weight is more than 2,050 Gm. and if the temperature is over 96 F., the infant is at once given an oil bath, is dressed in warmed clothing and is put into a crib. Weight and temperature are usually the only factors that determine whether an infant shall be placed in an incubator or a crib. The incubator is prepared in advance, so that the temperature and the humidity will be at operating levels when the infant is brought to the nursery.

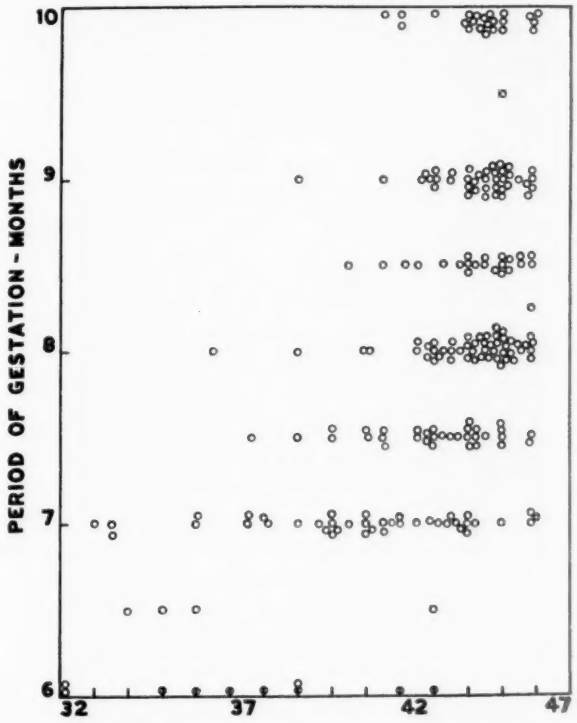

Fig. 3.—Correlation of length at birth of 220 premature infants with period of gestation.

The infant is not disturbed during the first twelve hours, unless there is some definite indication to the contrary, such as cyanosis. The temperature within the incubator is observed every four hours and is adjusted to between 85 and 90 F., according to the body temperature of the infant. A tank of oxygen is kept ready beside each incubator, equipped with an inverted funnel that can be placed over the nose and mouth of the infant if cyanosis develops. During the first year or two of this study a mixture of carbon dioxide and oxygen was used, but after some investigation it was found that oxygen alone was ade-

quate. If mucus collects in the pharynx, it is sucked out with a small soft rubber catheter attached to an aspirating bulb.

After the first twelve hours a routine of care is closely followed if the patient appears to be doing well. During the day feedings are given at three hour intervals; during the night, at three hour intervals at first and later at four hour intervals, when the infant has demonstrated ability to thrive. Usually before the feeding time, the diaper is changed and the temperature taken. All these procedures are carried out without removing the infant from the incubator. A daily oil bath is given until the infant's weight has reached 2,280 Gm.; then the infant receives oil and water baths on alternate days.

The technic of feeding and the type of food given are in some measure governed by the weight of the infant. During the first twelve hours nothing is fed by mouth, although occasionally, if severe dehydration is present, physiologic solution of sodium chloride is administered parenterally. All infants weighing less than 1,500 Gm. at birth are fed by gavage at first, and those weighing over 1,500 Gm. at birth are fed with a bottle. If the latter procedure is unsuccessful, gavage is resorted to until the bottle is accepted.

Irrespective of weight at birth each infant is given breast milk, which is supplied by his own mother when possible. A small amount is used at first, usually from 5 to 15 cc. at each feeding, according to the birth weight. The amount is gradually increased until an intake of from 130 to 160 calories per kilogram of body weight is achieved. Feeding with breast milk is continued for the first ten days of life, regardless of whether or not the infant's mother has an adequate supply. After this time, particularly when the mother's milk supply is inadequate, the feeding is usually changed to a dilution of evaporated milk and corn syrup. Naturally, the decision to make a change in diet is governed by individual circumstances. In general, an infant weighing over 1,500 Gm. at birth is fed a formula of evaporated milk and corn syrup, while an infant weighing under 1,500 Gm. at birth is fed breast milk until he has reached approximately this weight. Some of the larger infants continue to be fed breast milk if they are able to nurse without undue fatigue.

Due attention is paid to the administration of the accessory food factors in conjunction with adequate caloric requirements. With regard to vitamin D, special studies of rickets were conducted on many of the infants, and viosterol of two potencies, yeast milk and irradiated evaporated milk were tried. Since the problem of the prevention of rickets in premature infants is not yet solved, no one of these substances is employed as a routine procedure. Whichever source of vitamin D is used, its administration is started between the third and the sixth week

after birth, with the exception of the various types of vitamin D milk, which are given ten days after birth. Orange juice is usually given at 1 month of age. The infants receive at first 2 cc. a day; this amount is gradually increased to 30 cc. daily. Iron is first administered during the third or fourth week of life in the form of a 50 per cent solution of ferric ammonium citrate; the initial dose of 0.5 cc. is increased by 0.2 cc. daily until the infant is receiving 0.6 cc. per kilogram of body weight. Only infants weighing more than 1,500 Gm. receive this medication. During the first week of life, if severe dehydration is present an infant may be given one or more hypodermoclyses daily, at the ratio of 20 cc. per kilogram of body weight.

Although it is not my primary purpose in this paper to discuss the value of various types of feedings, there are some facts which merit attention. Of the 330 premature infants, 256 survived the initial ten days, during which all infants received breast milk. Feeding was continued as follows: 42 were given breast milk alone; 102 received complementary feeding; 112 were fed artificial formulas. Among those who continued to be fed breast milk alone, there were 2 deaths, a mortality of 4.8 per cent; among those who were fed partly with breast milk, there were 5 deaths, a mortality of 4.9 per cent; among those who were fed artificially, there were 13 deaths, a mortality of 11.6 per cent. Although comparison of mortality rates which are determined on the basis of so few deaths is scarcely justified without careful scrutiny of the cause of each death, it may be stated that the elimination of deaths due to possibly nonpreventable causes does not alter the essential truth suggested by the cited figures. Thus, 1 of the breast-fed infants died at 24 days of age of congenital syphilis; 2 of the infants given complementary feedings succumbed to the same disease, at 1½ months and 3 months, respectively; among the infants fed artificially, there was 1 death at 1 month, caused by congenital syphilis, and 1 death at 2 months, due to congenital atresia of the bile ducts. The mortality rates, then, suggest a tendency toward greater susceptibility to subsequent disease among the infants who were not receiving breast milk. The suggestion is strengthened by the fact that, in general, breast feeding was continued only for the weaker group of infants, i. e., those weighing less than 1,500 Gm. at birth.

CHARACTERISTICS OF THE SERIES OF INFANTS

In table 1 the distribution of the infants in this series is shown in four weight groups. In table 2 the distribution is shown in two weight groups, one composed of those infants whose weight at birth was over 1,500 Gm., and the other of those whose weight at birth was less than this figure. A study of the distribution of the infants in this series as

to sex and color brings out several interesting facts. The unusually high incidence of girls as compared with boys, 58.5 and 41.5 per cent, respectively, is a phenomenon which is difficult to explain but one which has been found to exist in other similar series. Capper [1] noted 56 per cent girls and 44 per cent boys; Wood [2] found 54.1 per cent girls and 45.9 per cent boys among 149 premature infants. The greater number of white than Negro infants, 66.4 per cent and 32.7 per cent, respectively, is accounted for by a similar distribution among the population which the Sloane hospital serves. The proportion of multiple births, 16.1 per cent, agrees closely with that recorded elsewhere. Capper [1] reported 15.5 per cent multiple births; Wood,[2] 16.1 per cent; Ylppö,[3] from 20 to 30 per cent; Hess and Chamberlain,[4] 25 per cent, and Comberg,[5]

TABLE 1.—*Premature Infants Classified in Four Groups According to Weight*

Weight at Birth	Number	Percentage
Total	330	
Under 1,000 Gm.	11	3.3
1,001-1,500 Gm.	56	17.0
1,501-2,000 Gm.	103	31.2
2,001-2,500 Gm.	160	48.5

TABLE 2.—*Premature Infants Classified in Two Groups According to Weight*

Weight at Birth	Number	Percentage
Total	330	
Under 1,500 Gm.	67	20.3
1,501-2,500 Gm.	263	79.7

16 per cent. In this series, in spite of the unequal distribution according to sex and color, the proportion of infants weighing over and under 1,500 Gm. at birth was relatively the same in each group. In table 3 the frequency distribution in terms of length is shown for the 250 infants for whom this measure was available.

The average period of hospitalization in this series was twenty and five-tenths days. If one excludes the 83 infants who died before leaving

1. Capper, A.: The Fate and Development of the Immature and of the Premature Child, Am. J. Dis. Child. **35**:443 (March) 1928.

2. Wood, C. L.: Unpublished data from the New Haven Hospital.

3. Ylppö, A.: Zur Physiologie, Klinik, und zum Schicksal der Frühgeborenen, Ztschr. f. Kinderh. **24**:1, 1919.

4. Hess, J., and Chamberlain, I. M.: Premature Infants: A Report of Two Hundred and Sixty-Six Consecutive Cases, Am. J. Dis. Child. **34**:571 (Oct.) 1927.

5. Comberg, M.: Ueber Schicksal und Entwicklung von Frühgeborenen zum Spiel- und frühen Schulalter, Ztschr. f. Kinderh. **43**:462, 1927.

the hospital, the average period is increased to twenty-eight and eight-tenths days. If the infants who survived the period of hospitalization are divided into two groups on the basis of size at birth, a decided difference is apparent: of 228 infants who weighed over 1,500 Gm. at birth, the average stay in the hospital was twenty-five and seven-tenths days; of 18 infants who weighed less than 1,500 Gm. at birth, the average stay was fifty-two days. The criterion for discharge from the hospital was a weight of 2,400 Gm. The longer period of hospitalization for the smaller infants reflects the slowness with which a satisfactory growth in weight was achieved. Only in rare instances was intercurrent infection responsible for prolonging the stay in the hospital.

TABLE 3.—*Distribution of Infants According to Length at Birth*

	Number	Percentage
Under 37 cm.	14	5.6
37-40 cm.	25	10.0
40-43 cm.	61	24.4
43-46 cm.	146	58.4
Over 46 cm.	4	1.6

TABLE 4.—*Mortality Rate During the Period of Hospitalization*

Birth Weight	Born	Died	Mortality, Percentage	Probable Error, Percentage
Total	330	83	25.1	1.6
Under 1,000 Gm.	11	11	100.0	8.8
1,001-1,500 Gm.	56	37	66.0	3.9
1,501-2,000 Gm.	103	23	22.3	2.9
2,001-2,500 Gm.	160	12	7.5	2.3

MORTALITY

Among the 330 infants there was a total of 94 deaths, a mortality of 28.5 per cent. Of this number 11 died after leaving the hospital in an apparently normal and healthy condition. The causes of death in this group are not relevant to this discussion. When the number of these deaths is subtracted from the total number, the corrected mortality becomes 25.1 ± 1.6 per cent. If from the number of this group of 83 who died in the hospital is subtracted the number of those who died from prematurity or injury sustained at birth within the first seventy-two hours of life, only 11 are left who died of theoretically preventable causes, making a corrected mortality of 4.4 per cent. Distribution of the deaths into several weight groups (table 4) shows that the usual higher mortality among the smaller infants obtains: 100 per cent mortality for those weighing less than 1,000 Gm. at birth and steadily decreasing mortality until the rate is only 7.1 per cent for those weigh-

ing over 2,000 Gm. at birth. In table 5 the relation between the age at death and the size at birth is demonstrated. Of the infants who weighed under 1,500 Gm. at birth, more than half died in the first twenty-four hours; the figure contrasts sharply with the number of deaths (1 in 16) for the same period among the infants who weighed over 1,500 Gm. It is clear that prenatal factors and the effects of prematurity per se have a predominant influence on the course of the life of the extremely small infant. That these factors continue for some time to diminish the prospect for survival is shown by the subsequent mortality rate, which is based on the number of deaths occurring during each age period among infants who had survived to the beginning of the period. In each age group the mortality rate is considerably higher for the infants who weighed less than 1,500 Gm. at birth than for those whose birth weight exceeded this figure. It is clear, furthermore, that an infant, especially if he is in the smaller size group, who has lived

TABLE 5.—*Mortality According to Age at Death*

	Under 1,500 Gm.			Over 1,500 Gm.		
		Mortality			Mortality	
Age at Time of Death, Days	Deaths, Number	Entire Group, Percentage	Among Survivors, Percentage	Deaths, Number	Entire Group, Percentage	Among Survivors, Percentage
0 to 1	37	55.3	55.3	16	6.1	6.1
1 to 5	6	8.9	20.0	12	4.5	4.9
5 to 31	4	5.9	16.7	3	1.1	1.3
31+	2	3.0	10.0	14	5.4	6.0

through the first day has a greatly improved outlook for ultimate survival.

In tables 6, 7 and 8 mortality in relation to single and multiple birth, color and sex is shown. One important fact requires special comment: The mortality rate of boys is consistently higher than that of girls; for the series as a whole the rates are 34.3 per cent and 24.4 per cent, respectively. The difference between these percentages is 3.12 times as great as the probable error of the difference, which means that the chances are 98 in a 100 that the difference observed does not result from random sampling.[6] The observation is consistent with that of Wood,[2] who noted a mortality of 56 per cent in boys and 34 per cent in girls; with that of Hess and Chamberlain,[4] who found a mortality of 60 per cent in boys and 48 per cent in girls, and with that of Blackfan,[7] who found the mortality higher in boys than in girls in every weight group.

6. Pearl, R.: Introduction to Medical Biometry and Statistics, ed. 2, Philadelphia, W. B. Saunders Company, 1930.

7. Blackfan, K. D.: The Premature Infant, Am. J. Dis. Child. **46**:1175 (Nov.) 1933

The mortality rates in relation to white and Negro infants and to single and multiple births in each weight group are similar to those of the entire group and to each other.

TABLE 6.—*Mortality in Relation to Single and Multiple Births*

	Total		Single Births		Multiple Births	
	Born	Died	Born	Died	Born	Died
Total						
Number	330	94	277	82	53	12
Mortality, percentage		28.5		29.5		22.6
Probable error, percentage		1.7		1.8		4.2
Under 1,500 Gm.						
Number	67	49	58	42	9	7
Mortality, percentage		73.1		72.4		77.8
Probable error, percentage		3.6		3.9		10.0
1,501 to 2,500 Gm.						
Number	263	45	219	40	44	5
Mortality, percentage		17.1		18.3		13.7
Probable error, percentage		1.6		1.7		3.8

TABLE 7.—*Comparison of Mortality of White with That of Negro Infants*

	White Infants		Negro Infants	
	Born	Died	Born	Died
Total				
Number	219	65	108	27
Mortality, percentage		29.7		25.0
Probable error, percentage		2.1		2.9
Under 1,500 Gm.				
Number	41	33	24	16
Mortality, percentage		80.5		66.7
Probable error, percentage		4.7		6.1
1,501 to 2,500 Gm.				
Number	178	32	84	11
Mortality, percentage		18.1		13.1
Probable error, percentage		1.9		2.8

Three infants are omitted because their color was not noted on their records.

TABLE 8.—*Comparison of Mortality of Male Infants with That of Female Infants*

	Boys		Girls	
	Born	Died	Born	Died
Total				
Number	137	47	193	47
Mortality, percentage		34.3		24.4
Probable error, percentage		2.6		2.1
Under 1,500 Gm.				
Number	29	23	38	26
Mortality, percentage		79.3		68.4
Probable error, percentage		5.6		4.9
1,501 to 2,500,Gm.				
Number	108	24	155	20
Mortality, percentage		22.2		12.9
Probable error, percentage		2.4		2.0

The mortality for each year of the five year period is shown in table 9. In general, the figures are self-explanatory. The columns for 1929 and 1934 represent, of course, only a partial experience: the last four months of 1929 and the first eight months of 1934. The percentage

of mortality during each year, both of the infants weighing over 1,500 Gm. at birth and of those weighing less than this amount, approximates closely the percentage of mortality for the entire period.

The seasonal mortality is shown in figure 4; the peak during the winter months coincides with the highest incidence of infection of the upper respiratory tract in the community at large. The significance of this fact is difficult to evaluate since extremely few of the deaths in the hospital were directly referable to acquired infection. Furthermore,

TABLE 9.—*Distribution of Mortality by Years*

	Total	1929	1930	1931	1932	1933	1934
Total							
Born	330	27	75	54	73	70	31
Died	94	7	21	11	23	20	12
Percentage of mortality	28.5	25.9	28.0	20.4	31.5	28.6	38.7
Probable error, percentage	1.7	5.9	3.5	4.2	3.6	3.7	5.5
Under 1,500 Gm.							
Born	67	6	12	6	23	13	7
Died	49	4	8	5	16	9	7
Percentage of mortality	73.1	66.7	75.0	83.3	69.5	69.2	100.0
Probable error, percentage	3.6	12.5	8.6	12.5	6.2	8.3	11.5
1,501 to 2,500 Gm.							
Born	263	21	63	48	50	57	24
Died	45	3	13	6	7	11	5
Percentage of mortality	17.1	14.3	20.6	12.5	14.0	19.3	20.8
Probable error, percentage	1.6	5.5	3.2	3.7	3.6	3.4	5.2

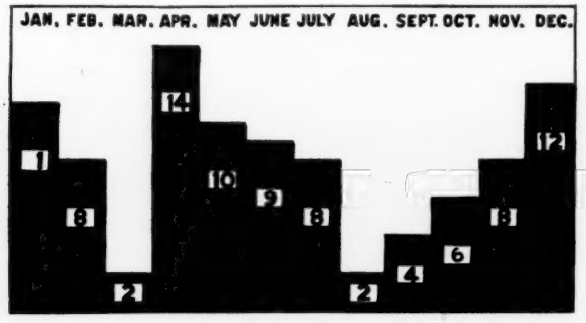

Fig. 4.—Distribution of mortality rate by months.

a large proportion of the deaths occurred during the first seventy-two hours of life. For these reasons it is clear that there can be no relation between seasonal mortality and incidence of infection.

In table 10 the causes of death grouped under five main types of disease are shown. Except in 15 cases in which no autopsy was performed, the classification was made on the basis of observations at postmortem examination. Among the infants weighing less than 1,500 Gm. at birth, the deaths were due almost entirely to prematurity and injury sustained at birth, with only a small percentage resulting from

infection. The infection was either omphalitis, with or without peritonitis, or syphilis. Among the infants weighing over 1,500 Gm. at birth the most frequent single cause of death was still prematurity, but infection had become second in importance. While several deaths were attributable to prenatal infection, by far the larger number resulted from intercurrent infection, usually of the upper respiratory or the gastro-intestinal tract. Intercurrent infection occurred chiefly among patients who died after leaving the hospital; prenatal infection predominated in those who died before discharge from the hospital. The apparent variation in the importance of these two factors in the two weight groups resulted merely from the fact that in the lower weight group a certain proportion succumbed to prenatal influences and injuries sustained at birth, leaving a smaller number to face the circumstances of postnatal life, whereas in the heavier weight group the prenatal

TABLE 10.—*Causes of Death of Ninety-Four Premature Infants*

	Total		Under 1,500 Gm.		1,501-2,500 Gm.	
	Number	Percentage	Number	Percentage	Number	Percentage
Total	94		49		45	
Prematurtiy	51	54.3	32	65.3	19	42.2
Birth injury	20	21.3	12	24.5	8	17.8
Infection	18	19.1	5	10.2	13	28.9
Congenital defects	1	1.1	..	....	1	2.2
Others	4	4.3	..	....	4	8.9

Autopsy was performed on 79 infants, and the following conditions were observed under the causes listed:
Prematurity: atelectasis, hyaline membrane of the lungs, diffuse hemorrhages of the viscera.
Birth injury: intracranial hemorrhage, hemorrhage of the adrenal glands.
Infections: omphalitis, pneumonia, peritonitis, syphilis.
Congenital defects: atresia of the bile ducts.
Others: anemia, aspiration of milk.

influences were minimized and a larger proportion of still inadequately equipped infants were left to face infections in their own homes.

The causes of death of the 11 infants who died while still in the hospital at an age greater than 72 hours are listed below. Unless the contrary is indicated, the observations were made at postmortem examination.

BABY J.—A girl weighing 1,210 Gm. at birth lived for four days. Necropsy showed evidence of acute fibrinous peritonitis and hyaline membrane of the lungs.

BABY G.—A girl weighing 1,070 Gm. at birth lived for two months and twenty-three days. Necropsy showed evidence of syphilitic osteochondritis of the femur, tibia, ribs and phalanges; osteomyelitis of the femur; syphilitic nephritis; early interstitial hepatitis, and early bronchopneumonia.

BABY W.—A boy weighing 1,040 Gm. at birth lived for twenty-six days. Necropsy showed evidence of syphilitic perichondritis, syphilis of the lungs and incarcerated indirect inguinal hernia on the right.

BABY K.—A girl weighing 1,204 Gm. at birth lived for eight days. Autopsy was not performed. During life the infant had frequent attacks of cyanosis, continuous vomiting and diarrhea. Continuous administration of oxygen was necessary.

BABY S.—A girl weighing 2,324 Gm. at birth lived for one week. Death was due to acute omphalitis, with septic thrombus of the cardiac auricle on the left.

BABY L.—A boy weighing 1,700 Gm. at birth lived for one month and twenty-six days. Autopsy was not performed. The patient was deeply jaundiced from the fourth day of life. The urine contained urobilin, and the stools showed no bile except on one occasion. The clinical diagnosis was congenital malformation of the bile ducts.

BABY G.—A boy weighing 1,970 Gm. at birth lived for one month and twenty-one days. Necropsy showed evidence of syphilis of the bones, erysipelas of the face and scalp and acute leptomeningitis, caused by Streptococcus haemolyticus.

BABY H.—A girl weighing 2,000 Gm. at birth lived for twenty-nine days. Autopsy was not performed. The patient was well during the first two weeks of life, after which diarrhea developed. She lost weight rapidly and became more dehydrated in spite of treatment. A postmortem culture of the blood yielded a hemolytic strain of Staph. aureus.

BABY M.—A boy weighing 1,740 Gm. at birth lived for five weeks. Postmortem examination showed evidence of hemorrhagic pneumonia, following the aspiration of milk.

BABY S.—A boy weighing 1,880 Gm. at birth lived for three weeks. Death resulted from hemorrhagic pneumonia, following the aspiration of milk.

BABY F.—A girl weighing 1,484 Gm. at birth lived for twenty-five days. The mother showed a positive Wassermann reaction. Necropsy revealed an abscess of the hypogastric artery and omphalitis.

CHARACTERISTICS OF GROWTH

No inclusive follow-up study of these infants was carried out, since observation was extended through only the first six months of life. Nevertheless, several characteristics of growth are suggested by the available data. In table 11 is recorded the average number of days required to regain the birth weight for the entire group and for the two subgroupings according to size. The longer time required for the lower weight group is in harmony with the indications already noted of inadequate preparation for extra-uterine existence. The effect of the weight at birth on the initial loss of weight could not be determined accurately because of the small number of infants, but there was a consistent tendency for a greater loss in those infants weighing less than 1,500 Gm. at birth. In several instances a determination of the number of days required to gain 500 Gm. showed the same tendency for infants weighing less than 1,500 Gm. at birth to lag behind those weighing over 1,500 Gm. at birth. In general, the infants in the higher weight group tended to require less than twenty days, and those in the lower weight group tended to require more than twenty days, to gain 500 Gm.

In table 12 the influence of the initial weight on the ability to gain weight over a longer period is shown. The well recognized tendency of small infants to "catch up" and approach the average weight curve of mature infants is apparent, even though the number of children observed is small. Among the 22 infants who weighed 4 or more times their birth weight at 6 months of age are all 12 infants who weighed less than 1,500 Gm. at birth and who were followed for this period. A relatively

TABLE 11.—*Average Number of Days Required to Regain the Birth Weight*

Birth Weight	No. of Infants	Days
Total	248	8.6
Under 1,500 Gm.	21	9.1
1,501-2,500 Gm.	227	8.2

TABLE 12.—*Weight at Six Months Compared with Weight at Birth*

	Under 1,500 Gm.	1,501-2,500 Gm.	Percentage
2 to 3 times birth weight	..	45	31.0
3 to 4 times birth weight	..	77	53.1
4 to 5 times birth weight	10	9	13.1
5 times birth weight	2	2	2.8
			100.0

TABLE 13.—*Congenital Abnormalities in 330 Premature Infants*

Syphilis	4
Malformation of the heart	2
Spina bifida	2
Clubbed feet	2
Atresia of bile ducts	1
Hydrocephalus	1
Harelip; cleft palate	1
Polydactylism	1
Atelectasis, one lung	1
Duodenal atresia	1
Total	16

small number, 10, of the infants who weighed more than 1,500 Gm. at birth fall into this group, the vast majority, 118, weighing from 2 to 4 times their initial weight at 6 months of age.

The incidence of congenital abnormalities among the infants of this series is shown in table 13. Such conditions as phimosis and tongue-tie have been omitted purposely because of their frequency and doubtful significance. Umbilical hernia was omitted because of the difficulty in separating a congenital condition from one resulting from an umbilical wound at birth.

SUMMARY

The current methods of care, treatment and feeding of premature infants born in the Sloane Hospital for Women are described.

In the five years from Sept. 1, 1929, to Aug. 31, 1934, among 10,163 consecutive births, 330 infants weighing less than 2,500 Gm. were born in the ward service, an incidence of 3.2 per cent.

There was a tendency toward a greater susceptibility to disease and toward a higher mortality rate in those premature infants receiving little or no breast milk after the first ten days of life.

There were more girls in this series than boys, 58.5 per cent of the former and 41.5 per cent of the latter.

The period of gestation based on the mother's history is a much less accurate and less satisfactory method of evaluating immaturity than the weight or the length of the infant at birth.

The mortality rate for the entire group of 330 infants was 28.5 per cent; the corrected mortality rate which included only those infants who died in the hospital was 25.1 per cent; the corrected mortality rate which considered only those who died in the hospital after the first seventy-two hours was 4.4 per cent.

The mortality rate among boys was significantly higher than among girls, not only in the entire group of 330 infants but also in the higher and lower weight groups.

Prematurity per se is the most common single cause of death, with injury sustained at birth the next most common in those infants weighing less than 1,500 Gm. at birth and infection the next most common in those infants weighing over 1,500 Gm. at birth.

Premature infants weighing less than 1,500 Gm. at birth tend to develop more slowly at first than do those weighing over 1,500 Gm. at birth, but they do tend to approach the average weight of mature infants by the age of 6 months.

INVOLUTION OF THE ADRENAL GLANDS IN NEWLY BORN INFANTS

A BIOCHEMICAL INQUIRY INTO ITS PHYSIOLOGIC SIGNIFICANCE

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The imposing size of the adrenal bodies in the human fetus and in the newly born infant has long attracted the attention of anatomists. The first detailed histologic description of the involutional process whereby these glands are converted into the mature but relatively smaller organs of childhood and adult life was published by Thomas [1] in 1911. In an investigation of the response of the adrenal glands during infections, Thomas called attention to the fact that these structures normally undergo extensive morphologic reorganization during the first year of life: The inner zone of the cortex (zona reticularis), which is relatively wide and conspicuously hyperemic at birth, suffers complete degeneration and is encroached on and replaced by the rapidly growing medullary portion of the gland. More exact information concerning the details of the maturation of the adrenal glands was contributed by the researches of Kern,[2] Kawamura,[3] Landau,[4] Lewis and Pappenheimer [5] and Scammon.[6] The results of previous investigations were summar-

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1. Thomas, E.: Ueber die Nebenniere des Kindes und ihre Veränderungen bei Infektionskrankheiten, Beitr. z. path. Anat. u. z. allg. Path. **50**:283, 1911.

2. Kern, H.: Ueber den Umbau der Nebenniere im extrauterinen Leben, Deutsche med. Wchnschr. **37**:971, 1911.

3. Kawamura, R.: Die Cholesterinverfettung (Cholesterinsteatose), Jena, Gustav Fischer, 1911, p. 136.

4. Landau, M.: Die Nebennierenrinde, Jena, Gustav Fischer, 1915; cited by Aschoff.[7]

5. Lewis, R. W., and Pappenheimer, A. M.: A Study of the Involutional Changes Which Occur in the Adrenal Cortex During Infancy, J. M. Research **34**:81, 1916.

6. Scammon, R. E.: The Prenatal Growth and Natal Involution of the Human Suprarenal Glands, Proc. Soc. Exper. Biol. & Med. **23**:809, 1926.

ized by Aschoff [7] in 1924. The morphologic aspects of the process were again reviewed in 1934, by Yasukawa,[8] a pupil of Aschoff.

The phenomenon is encountered only in man. As early as the fourth month of fetal life, that zone of the primitive adrenal cortex which is destined to be reconstructed, namely, the "primary" inner zone, exhibits hyperemia and becomes infiltrated by lipoid material; these characters grow progressively more evident up to the time of birth, when the hyperemia is maximal. The true degeneration, which commences at birth, affects this zone and is characterized by widespread fatty infiltration, loss of substance, disappearance of hyperemia and proliferation of connective tissue; moderate hemorrhage may occur, even under circumstances which preclude the possibility of trauma occurring at birth, that is, in the case of infants delivered by cesarean section. Opinions differ concerning the length of time during which degeneration continues. Thomas asserted that the whole process of involution requires about one year. Lewis and Pappenheimer encountered no evidence of active degeneration beyond two weeks after birth and no signs of regeneration up to the third year of life. According to Scammon, the glands lose weight rapidly during the first two weeks of life and then more gradually during the subsequent month, finally arriving at stationary weight by the end of the sixth week after birth. Yasukawa found the rudiments of the mature stratified structure to be clearly discernible by the end of the sixth week of life; he affirmed that the most active degeneration takes place during the first weeks after birth. Definite information is lacking concerning the process of regeneration and the final conversion of the immature gland into the mature organ. This problem need not be considered here.

Numerous theories have been advanced concerning the physiologic implications of this phenomenon. The majority of these theories relate to the medullary portion of the gland; hypotheses pertaining to the transformation of the cortex emphasize its relation to the utilization of oxygen [9] and to the production of heat [10] by the developing organism.

In view of the recent important advances in knowledge concerning the relation of the hormone, or hormones, of the adrenal cortex to the

7. Aschoff, L.: Lectures on Pathology, New York, Paul B. Hoeber, Inc., 1924, p. 101.

8. Yasukawa, Y.: Zur Frage der Nebenniereninvolution, Endokrinologie **14**:161, 1934.

9. Goldzieher, M. A., and Gordon, M. B.: Pseudopneumonia Infantum: Ein durch akuten Nebennierenausfall bedingtes Krankheitsbild, Klin. Wchnschr. **12**: 270, 1933.

10. Marine, D. W.; Lowe, B., and Cipra, A.: Influence of Glands with Internal Secretion on the Respiratory Exchange: VII. The Possible Influence of Suprarenal Involution in New Born Infants on Heat Production, J. Metabolic Research **2**:329, 1922.

sodium and water economy of the body, it has seemed worth while to investigate this aspect of the physiology of the neonatal period. Specifically, the object of this study was to determine whether the changes in the blood which are found in patients with Addison's disease or in dogs suffering from experimentally produced adrenal insufficiency can be demonstrated in normal infants during the first three weeks of life.

As summarized in Loeb's recent review,[11] the pathologic consequences of privation of the adrenal cortex are, in part, as follows: first, an increase in the excretion of sodium through the kidneys, followed by a fall of the concentration of sodium in the blood plasma. We quote the following excerpt from Loeb:

> As sodium is lost from the body there is an increased, though not equivalently increased, excretion of water. . . . The following changes may be ascribed to the loss of sodium with its accompanying dehydration: (1) decrease in concentration of sodium in the blood with a fall in blood bicarbonate or chloride or both; (2) increase in plasma protein concentration and in the oxygen capacity of the blood; (3) decrease in plasma volume; (4) decrease in rate of blood flow; (5) increase in excretion of chloride; (6) loss of weight. In turn, this resultant state of dehydration and shock is also probably of importance in augmenting the following manifestations of adrenal insufficiency: (7) refusal of food; (8) vomiting; (9) muscular weakness; (10) diminution in blood pressure; (11) diminution in metabolic rate; (12) increase in total non-protein nitrogen of the blood and often in urea, and increase in phosphate and sulphate in advanced stages, and (13) anuria when shock is extreme.

EXPERIMENTAL PROCEDURE

For the purposes of this study we chose to measure the concentration of sodium in the plasma, the specific gravity of the plasma and the relative cell volume of whole blood. For comparison, the amount of total base in the plasma was determined whenever the amount of the sample permitted; the nonprotein nitrogen content of the whole blood was estimated in about one third of the cases; in all instances hemoglobin was determined by Sahli's method, but the inaccuracy of the results in relation to hematocrit determinations caused us to discard the data.[12]

Since it was not possible to obtain samples of blood from the same infants daily throughout the period of three weeks, we chose to assemble average values for each day of the period by obtaining from one to four specimens of blood at different times from each of a series of seventy-two infants. All the patients studied were born in the Sloane Hospital for Women. They were largely breast fed, although many received complementary or supplementary feedings of evaporated cow's milk, water and corn syrup. We did not attempt to estimate the quantity of sodium chloride which the subjects ingested daily. All the patients were in good health. Although mild transient jaundice occurred

11. Loeb, R. F.: The Adrenal Cortex, J. A. M. A. **104**:2177 (June 15) 1935; reprinted in Glandular Physiology and Therapy, Chicago, American Medical Association, 1935, chap. 20, p. 299.

12. These specimens also provided material for a study by W. M. Sperry (Cholesterol of the Blood Plasma in the Neonatal Period, Am. J. Dis. Child. **51**:84 [Jan.] 1936).

in about one third of the patients studied, its presence did not appear to influence the results of the determinations.

From seven infants samples of blood were obtained immediately after birth by puncture of the umbilical vein between two clamps applied to it about 1 meter apart; all other specimens were obtained by venipuncture in the antecubital fossa. It was usually necessary to employ considerable stasis in order to obtain the samples of from 6 to 8 cc. necessary for the determinations. We found it impracticable to collect the blood under oil. Approximately 1 mg. of dry heparin per cubic centimeter of blood was used to prevent coagulation. The sodium content was determined in 0.5 cc. aliquots of plasma by precipitation as sodium uranyl zinc acetate, according to the directions of Butler and Tuthill.[13] The average values for each day, expressed originally in milliequivalents of sodium per liter of plasma, were converted into milliequivalents per liter of plasma water by use of the formula proposed by McLean and Hastings,[14] namely: water (in grams per hundred cubic centimeters of plasma) = 99 —07.5 P (P equals grams of protein per hundred cubic centimeters). The specific gravity of the plasma was determined by the falling drop method of Barbour and Hamilton;[15] the values for specific gravity were converted into grams of protein per hundred cubic centimeters of plasma by use of the formula of Moore and Van Slyke,[16] namely, protein = 343 (specific gravity —1.007). The accuracy of this prediction was recently confirmed in this laboratory by Weech, Reeves and Goettsch.[17] For determining the relative volume occupied by the red cells we employed hematocrit tubes with a bore of 1 mm. and a length of 14 cm., divided into 100 equal linear units. The tubes were centrifuged at high speed (approximately 2,500 revolutions per minute) for thirty-five minutes; this produced a constant volume of the packed erythrocytes. The total base was determined, in samples of 0.5 or of 1 cc., according to Hald's gravimetric modification of the benzidine method.[18] Nonprotein nitrogen was determined by the method of Folin and Wu,[19] with samples of 0.5 cc. The measurements of the sodium content of the plasma and of the cell volume were performed in duplicate. The probable error of measurement (PE_M) of eighty-one duplicate determinations of sodium was $\pm$ 0.7 milliequivalents of sodium per liter of plasma; the readings of hematocrits filled from the same

13. Butler, A. M., and Tuthill, E.: An Application of the Uranyl Zinc Acetate Method for Determination of Sodium in Biological Material, J. Biol. Chem. **93**:171, 1931.

14. McLean, F. C., and Hastings, A. B.: The State of Calcium in the Fluids of the Body: I. The Conditions Affecting the Ionization of Calcium, J. Biol. Chem. **108**:285, 1935.

15. Barbour, H. G., and Hamilton, W. F.: The Falling Drop Method for Determining Specific Gravity, J. Biol. Chem. **69**:625, 1926.

16. Moore, N. S., and Van Slyke, D. D.: The Relationships Between Plasma Specific Gravity, Plasma Protein Content and Edema in Nephritis, J. Clin. Investigation **8**:337, 1929.

17. Weech, A. A.; Reeves, E. B., and Goettsch, E.: The Relationship Between Specific Gravity and Protein Content in Plasma, Serum and Transudate from Dogs, J. Biol. Chem. **113**:167, 1936.

18. Hald, P. M.: The Determination of the Bases of the Serum and Whole Blood, J. Biol. Chem. **103**:471, 1933; A Note on the Gravimetric Determination of Total Base of Serum and Blood, ibid. **105**:675, 1934.

19. Folin, O., and Wu, H.: A System of Blood Analysis, J. Biol. Chem. **38**:81, 1919.

sample of blood and centrifuged simultaneously were always in close agreement. The reported values for specific gravity represent the mean of determinations made with from 3 to 5 separate drops of both the standard solution and the plasma. In a series of sixty-two specimens of plasma we investigated the reliability of the falling drop method in comparison with that of the pyknometric method, using bottles which held approximately 2 cc. In this manner we

*Mean Values and Standard Deviations**

Day of Life	Weight in Percentage of Birth Weight (3,467 Gm.)	Hematocrit Reading, Vols. per 100 Cc.	Specific Gravity	Protein, Gm. per 100 Cc.	Sodium, M. Eq. per Liter of Plasma	Sodium, M. Eq. per Liter of Plasma Water	Total Base, M. Eq. per Liter of Plasma	Nonprotein Nitrogen, Mg. per 100 Cc. of Whole Blood
Cord Blood	100 (7)	51.7 (7) ±3.6	1.0241 (7) ±0.0042	5.88 (7) ±0.34	141.6 (7) ±5.5	149.8	159 (5)	....
1	97.8 (12) ±1.9	57.2 (12) ±5.9	1.0263 (12) ±0.0036	6.61 (12) ±0.41	144.6 (12) ±3.1	153.8	157 (5)	42.2 (5)
2	96.3 (10) ±2.6	60.8 (10) ±4.0	1.0256 (10) ±0.0041	6.26 (10) ±0.58	144.6 (10) ±3.1	153.4	....	46.3 (6)
3	92.1 (6) ±3.4	65.2 (6) ±6.3	1.0264 (6) ±0.0016	6.78 (6) ±0.38	145.0 (5) ±5.4	154.4	160 (2)	36.3 (1)
4	88.2 (5) ±5.3	61.3 (5) ±5.0	1.0283 (5) ±0.0128	7.32 (5) ±1.38	143.5 (5) ±6.2	153.5	171 (2)	34.1 (1)
5	94.0 (5) ±3.5	58.8 (5) ±4.6	1.0263 (5) ±0.0065	6.55 (5) ±0.68	143.7 (5) ±4.4	152.8	153 (2)	33.2 (1)
6	95.0 (9) ±4.3	54.9 (8) ±5.2	1.0256 (8) ±0.027	6.37 (8) ±0.35	145.9 (7) ±4.2	154.9	159 (2)	38.4 (5)
7	96.8 (8) ±3.2	54.8 (8) ±4.4	1.0253 (8) ±0.0032	6.26 (8) ±0.31	144.1 (7) ±3.0	152.9	158 (2)	40.5 (3)
8	94.8 (9) ±7.4	56.0 (9) ±4.8	1.0261 (9) ±0.0070	6.55 (9) ±0.69	145.0 (7) ±3.1	155.9	155 (2)	39.0 (5)
9	98.2 (10) ±5.0	54.0 (10) ±6.2	1.0252 (10) ±0.0063	6.26 (10) ±0.70	144.3 (10) ±4.0	152.5	158 (6)	40.5 (4)
10	97.6 (9) ±4.5	55.4 (9) ±4.9	1.0249 (9) ±0.0049	6.00 (9) ±0.56	146.1 (9) ±4.7	154.5	155 (2)	36.5 (2)
11	97.3 (5) ±1.4	55.6 (5) ±4.9	1.0248 (5) ±0.0039	6.16 (5) ±0.48	145.2 (5) ±2.9	154.0	155 (4)	37.5 (2)
12	100.3 (7) ±5.3	47.7 (6) ±4.3	1.0248 (6) ±0.0023	6.09 (6) ±0.27	145.6 (7) ±4.2	154.2	160 (1)	39.5 (5)
13-14	99.8 (6) ±7.9	53.4 (4) ±2.9	1.0248 (6) ±0.0044	6.12 (6) ±0.49	142.2 (6) ±3.9	150.6	153 (2)	46.4 (1)
15-17	100.4 (5) ±2.0	47.2 (5) ±4.1	1.0255 (5) ±0.0047	6.32 (5) ±0.45	144.1 (5) ±3.4	152.7	153 (3)	33.2 (2)
18-25	111.8 (6) ±6.4	51.5 (6) ±5.1	1.0255 (6) ±0.0075	6.33 (6) ±0.83	146.5 (6) ±4.9	155.0	171 (1)	34.5 (2)
Total cases	119	115	117	117	113		41	45

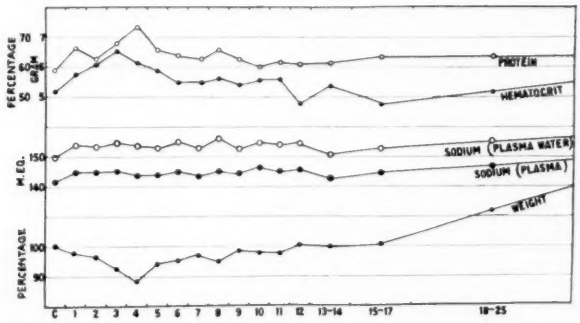
* The figures in parentheses refer to the number of determinations. The number of analyses of total base and of nonprotein nitrogen is too small to impart significance to the calculation of standard deviation.

satisfied ourselves that the mean value obtained from several drops compares favorably, as regards accuracy, with the mean value obtained by pyknometric determinations performed in duplicate. With few exceptions, the analyses for total base and nonprotein nitrogen were made singly.

OBSERVATIONS

The table contains the data derived from this experiment. The mean values for the separate days are recorded, together with the standard deviations for those values.

The chart expresses graphically the fluctuations of the sodium and the protein content of the plasma, as well as the relative cell volume and body weight, during the neonatal period. The weight curve reflects the loss of mass which occurs so uniformly in newly born infants. In our patients the average decrease amounted to 12 per cent of the birth weight; the maximum loss was reached on the fourth day of life and was followed by gradual gain. During the first four days of life the decline in weight was accompanied by evidence of an increase in the concentration of the cellular and plasma protein fractions in the blood, attested to by a rise of 18 per cent in the relative volume of the red cells and an increase of 24 per cent in the concentration of protein in the plasma. Despite these alterations, the concentration of sodium both in the plasma and in the plasma water remained conspicuously constant. In seven samples of cord blood the concentration of sodium was 141.6



The simultaneous variations of plasma sodium, plasma protein, relative cell volume and body weight during the first three weeks of life. Sodium is expressed both in milliequivalents per liter of plasma and in milliequivalents per liter of plasma water. Body weight is expressed in terms of the percentage of gain or loss with reference to the weight at birth. *C* represents cord blood. The numerals along the abscissa represent days of life.

$\pm$ 5.5 milliequivalents per liter of plasma; in five samples taken on the fourth day of life the concentration was 143.5 $\pm$ 5.4 milliequivalents per liter of plasma. Significant variation in the concentration of sodium was not encountered during the whole period covered by the study. The mean concentration of sodium from the first to the twenty-fifth day of life was 144.8 milliequivalents per liter of plasma; the standard deviation amounted to only $\pm$ 4.1 milliequivalents. The dependability of these uniform values is supported by the lack of variation in the concentration of total base in the plasma; the three figures of 171 milliequivalents encountered on the fourth day and again between the eighteenth and the twenty-fifth day must be regarded with suspicion as to technical accuracy.

The concentration of nonprotein nitrogen in the whole blood is considered to be a somewhat more sensitive index of privation of the adrenal cortex than is the sodium content, although it is admittedly less specific. Our small series of determinations revealed somewhat elevated values on the first and second days of life, with a tendency to fall to normal thereafter; the results of our determinations, in close agreement with those obtained by Sedgwick and Ziegler,[20] fail to suggest deficiency of the cortical hormone.

From eleven of the seventy-two infants we obtained three or four samples of blood on separate days. The curves of the concentrations of sodium and protein in the plasma and of cell volume in the case of individual subjects exhibited close resemblance to the composite curves presented in the chart. In no case did we encounter values which would justify designating the infant as unusual or abnormal.

SUMMARY AND CONCLUSIONS

Determinations of the sodium content and the specific gravity (protein content) of the plasma, the cell volume and the nonprotein nitrogen content of the whole blood and the amount of total base in the plasma were made on seven samples of blood from the umbilical vein and in one hundred and six specimens of venous blood obtained from seventy-two healthy infants within the first three weeks of life.

Despite the temporary increase which these infants exhibited with reference to the volume of erythrocytes and the level of plasma protein, the concentration of sodium and of total base in the plasma remained normal and constant during the period of the study, at levels identical with those found in healthy children and adults. The concentration of nonprotein nitrogen was inconspicuously elevated during the first few days of life; at no time was it high enough to suggest functional insufficiency of the adrenal cortex.

We have been unable to demonstrate in newly born infants, during the period when rapid involutional changes are occurring in the cortex of the adrenal glands, biochemical changes of the sort found in human beings with Addison's disease or in animals deprived experimentally of the adrenal cortex.

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20. Sedgwick, J. P., and Ziegler, M. R.: The Nitrogenous and Sugar Content of the Blood of the New-Born, Am. J. Dis. Child. **19**:429 (June) 1920.

EPIDEMIC LYMPHOCYTIC MENINGO-ENCEPHALITIS

A REPORT OF THIRTY-SEVEN CASES OCCURRING IN PHILADELPHIA

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This is a report of a series of thirty-seven cases of epidemic lymphocytic meningo-encephalitis occurring in Philadelphia in the summer of 1935. The children were admitted to the children's department of the Philadelphia General Hospital, in the service of Dr. William N. Bradley, between the dates of July 27 and September 15. During the same period a total of one hundred and nineteen patients were admitted to the wards with all types of complaints, so that this series comprised approximately one third of the total patients admitted. In addition, twenty-six patients were admitted to the adult medical service with apparently the same condition.

In general, these patients presented the picture of abortive poliomyelitis, and during the same time there were undoubtedly cases of poliomyelitis in and about Philadelphia. None of our children or adults displayed paralysis, nor did we admit a patient with poliomyelitis in the active phase during this period.

There were numerous similar cases about Philadelphia during this time. One of us (E. L. N.) saw seven patients with the condition in private practice. Other cases were reported in a survey of Philadelphia hospitals, although an accurate estimate cannot be made because of the confusion with poliomyelitis in the reports.

The disease was communicable. There was considerable familial incidence. Seven of our thirty-seven patients came from three households. We were able to interrogate the members of twenty-one families from one to two months after the patient's discharge. Five families reported other cases in the same household. Four families reported an apparently similar condition among playmates.

The two following histories are the most striking:

REPORT OF CASES

CASE 6 (E. S.).—On July 29 a brother of the patient, 5 years old, complained of headache, vomiting, fever and abdominal pain. The duration of the illness was four days.

On August 2 the onset of the patient's (E. S.) symptoms occurred. He was admitted to the hospital on August 6.

On August 8 a brother, 3 years old, complained of headache, vomiting and fever. The duration of the illness was fourteen days.

On August 13 a girl employed in the same house complained of headache, vomiting and fever. The duration of the illness was fourteen days.

On August 19 three adult sisters of this girl complained of similar symptoms as well as of photophobia. The duration of the illness was fourteen days.

CASE 19 (W. H.).—On August 14 the onset of the patient's (W. H.) symptoms occurred. He was admitted to the hospital on August 16.

On August 19 a brother, 4 years old, and his mother complained of headache, vomiting and chills.

On August 21 a brother, 2 years old, suffered from headache, vomiting and fever. The duration of the illness was four days.

On August 23 a sister, 7 years old, and an uncle, 28 years old, complained of headache, vomiting, fever and pains in the legs and back.

The patient's mother stated that similar cases were prevalent in the neighborhood.

The dates of admission were fairly evenly spaced (table 1). The majority of patients were admitted during the month of August.

The ages were uniformly distributed, ranging from 1 month to 11 years (table 2). Patients over 12 years of age are not admitted to the children's ward.

There were twenty-one boys and sixteen girls. There was no noteworthy racial factor.

The patients were admitted to the hospital with the following diagnoses: sixteen with meningitis (one of these patients with tuberculous meningitis); six with poliomyelitis; two with pneumonia; one with tetanus; three with abdominal disorders, and nine "for study."

COURSE

Recovery was rapid and uneventful in thirty-six cases. In case 24 the patient died. This case is included in the series and is considered to be an instance of a fulminating type of the disease. This case and the pathologic changes observed will be described separately.

Headache, fever and vomiting occurred in practically every case. Of these symptoms, headache was most striking to the observer.

In a municipal hospital it is difficult to obtain an accurate history preliminary to the admission of the patient. From our data it appears that the duration of the disease was usually between three and six days (table 3). Three patients apparently recovered in two days, and in one the condition persisted for nine days.

Many of the children appeared to be profoundly ill, while others laughed and joked as the physician made the examination. Many were obviously suffering from intense headache.

Eleven children were described as drowsy, somnolent, listless or stuporous. Six were described as showing an increase in irritability.

The onset of the disease was abrupt in some cases; in others it was insidious, with preliminary headache. Case 36 (M. S.) is of interest. The patient, an 8 year old girl, had previously been admitted to the

TABLE 1.—*Distribution of Dates of Admission to the Hospital of Thirty-Seven Patients*

Dates	No. of Cases	Dates	No. of Cases
July 27	1	August 24	3
30	2	25	2
August 1	1	26	2
6	2	28	1
7	2	29	1
8	4	30	2
10	1	September 3	1
11	1	4	1
12	2	9	1
13	2	12	1
16	2	15	1
21	1		

TABLE 2.—*Distribution of Ages of Thirty-Seven Patients with Meningo-Encephalitis*

Age	No. of Cases	Age	No. of Cases
1 month	1	6 years	3
6 weeks	1	7 years	4
1 year	0	8 years	4
2 years	3	9 years	3
3 years	2	10 years	1
4 years	3	11 years	7
5 years	5	12 years	0

TABLE 3.—*Duration of the Acute Attack of Meningo-Encephalitis in Thirty-Six Cases*

Duration	No. of Cases	Duration	No. of Cases
1 day	0	6 days	5
2 days	4	7 days	3
3 days	8	8 days	1
4 days	7	9 days	1
5 days	7		

hospital with the diagnosis of chorea. The choreiform movements almost entirely disappeared but became accentuated seven days prior to her admission with lymphocytic meningo-encephalitis. Other symptoms, such as headache, vomiting and fever, did not appear until seven days after the accentuation of the choreiform movements.

The subsidence of the headache after spinal drainage was dramatic.

EVIDENCE OF SEQUELAE

Twelve children in this series of cases were studied by Dr. R. H. Thompson, of the neurological staff, for evidence of organic neurologic sequelae. This preliminary study was made in February 1936, approximately six months after the acute period. Evidence of organic changes in the brain were present in all patients who were examined, but since this is a preliminary report of a more elaborate survey, only a brief summary of the observations will be given.

	No. of Cases
Impaired convergence	9
Impaired tendon reflex activity	9
Choreiform movements	4
Choreiform restlessness	3
Impaired automatic movements of the upper extremities	3
Change in personality	1
Hyperhidrosis	1
Enuresis	1
Somnambulism	1

None of these conditions as far as could be ascertained was noted prior to the acute illness.

SYMPTOMS AND SIGNS

Fever.—Every patient had some elevation of temperature. The lowest recorded temperature was 99 F.; the highest, 105 F. In the majority of cases the temperature reached a height of from 101 to 102 F., although one third of the patients attained a peak of 103 F. or over. The duration of the fever varied widely, from two to seven days. After admission to the hospital the temperature of the majority of patients returned to normal in one or two days, although in one case the elevation persisted for five days. The accuracy of the reports of the duration of fever prior to admission is open to question, but from twenty-two cases in which the data are fairly definite it seems that the fever usually lasted between three and four days in all.

Headache.—The most striking symptom of the disease was headache. Of the thirty-five children of sufficient age for observation, all but three had headache. The headache was usually severe and tended to be persistent. It was most frequently localized in the frontal region, although sometimes it was situated at the top of the head. It usually preceded the vomiting and in many cases the fever. Withdrawal of spinal fluid almost always afforded prompt relief.

Vomiting.—Thirty-two children vomited. In about one third of the cases (twelve) the vomiting persisted for two or more days. The vomiting did not appear to be secondary to gastro-enteritis. Several

children showed abdominal tenderness on palpation, and nine complained of abdominal pain, but in only two cases were stools that varied from the normal noted.

Eyes.—Seven patients showed some degree of photophobia. Examination of the eyegrounds of twelve children gave negative results, except in three cases in which a slight blurring of the disk was noted. Several children had mild conjunctivitis.

Nose and Throat.—Although there was no noteworthy inflammation of the nose and throat, we noted a slight inflammation in fifteen cases.

Chills.—Four children had chills.

Nervous System.—Twenty-seven children either had nuchal rigidity or complained of pain on bending the spine. Of these, fifteen demonstrated nuchal rigidity and nineteen had a positive spinal sign.

Alteration in reflexes was not striking or uniform. In fifteen children the deep reflexes were hypotonic; in two they were hypertonic, and in the cases of three description was omitted. The tendency was toward a decrease in response. Fourteen children showed a positive Kernig sign. Other changes in the reflexes were not particularly noteworthy. Two patients showed mild tremors of the arms. In only one case was a positive Babinski sign elicited.

LABORATORY DATA

The most interesting data were provided by examination of the spinal fluid (table 4), which was made in all thirty-seven cases. More than one examination was made in twenty-seven cases.

The total cell counts varied so widely that it is impracticable to attempt to average them, especially since variations occurred with the day of the disease. As is seen from the chart, in the majority of instances the spinal fluid yielded in the neighborhood of 100 cells, and in only three cases was there a count of less than 40 cells. The highest total count was 650 cells (case 11).

The cells were chiefly lymphocytes. In twenty-six determinations made in nineteen cases, the cells were 100 per cent lymphocytes. In one case (case 36) the count yielded chiefly neutrophils. In two cases (case 3 and case 25) the count yielded an equal distribution between neutrophils and lymphocytes, although a second examination of the fluid in case 3, performed two days later, showed an increase in the number of lymphocytes.

The tendency was for the number of neutrophils to be higher in earlier counts than in subsequent counts. When a total increase in the number of cells occurred, as it did in later counts in six cases, the increase was in lymphocytes.

TABLE 4.—*Estimated Date from Onset on Which Spinal Fluid in Thirty-Seven Cases Was Examined and Results of Examination*

Case	Date	Day From Onset	Pressure	No. of Cells per Cu. Mm.	Differential			Qualitative Globulin	Quantitative Dextrose, Mg. per 100 Cc.	Quantitative Chloride, Mg. per 100 Cc.
					Neutrophils	Lymphocytes	Endothelial Cells			
1	7/27	1	10	9						
	8/ 5	10	5	150	0	95	5	1		
	8/14	19	4	17	0	100	0	1		
2	7/31	8	12	130	24	66	10	3	72	696
	8/16	24	..	0						
3	7/31	3	..	36	50	50	0	1		
	8/ 2	5	8	130	1	94	5	3		
	8/14	17	8	15	0	100	0	1		
4	8/ 1	4	8	65	3	84	13	1		
	8/14	17	10	14	0	100	0	1		
5	8/ 8	4	14	40	0	100	0	1	59	680
	8/13	9	10	30	0	100	0	1		
6	8/ 8	6	8	220	0	100	0	1	..	694
	8/14	12	7	360	0	100	0			
7	8/ 8	2	9	100	0	100	0	1	59	702
	8/13	7	8	55	0	100	0			
8	8/ 9	2	10	100	0	100	0	1		
9	8/ 9	3	8	25	0	100	0	1	54	708
	8/14	8	4	38	0	100	0			
10	8/ 8	2	20	300	0	100	0	1	59	714
	8/15	9	5	150	0	100	0	1		
11	8/ 8	1	17	650	0	100	0	1	72	702
	8/17	10	..	20	0	100	0			
12	8/ 9	4	11	270	0	100	0	1	84	687
	8/14	9	8	65	0	100	0			
13	8/16	6	8	80	0	100	0			
14	8/12	3	14	30	0	100	0	..	68	
	8/23	14	..	0						
15	8/13	2	10	14	0	100	0	1		
16	8/18	7	8	40	0	100	0	1		
17	8/13	4	6	500	20	80	0	3	68	710
	8/20	11	..	51	0	100	0	1		
18	8/13	3	..	290	20	80	0			
19	8/16	2	10	100	20	80	0	1		
	8/22	8	8	26	0	100	0	1		
20	8/17	3	10	300	20	80	0	1		
	8/23	9	6	10	..	...	..	1		
21	8/21	4	12	72	24	72	4	1		
	8/22	5	..	141	10	80	10	1	68	690
22	8/25	6	4	24	..	...	..	1		
23	8/25	1	10	80	35	65	0	2		
	9/ 2	9	10	49	0	100	0	1		
24	8/24	1	14	92	..	...	..	..	..	675
25	8/25	1	14	130	50	50	0	2		
	9/ 3	10	12	12						
26	8/25	4	14	70	10	90	0	1		
	9/ 2	12	..	3	..	...	..	1		
27	8/26	1	6	37	..	...	..	1		
	8/27	2	..	65	10	90	0	..	134	692
28	8/27	4	6	70	0	100	0	1		
	9/12	20	..	6	..	...	..	1		
29	8/28	1	10	76	14	68	6	2		
	9/ 3	7	..	24	..	...	..	2		
30	8/29	4	5	40	12	88	0	1		
	9/ 5	11	..	13	..	...	..	2		
31	8/31	1	8	87						
	9/ 5	6	..	16	..	...	..	1		
32	8/30	1	4	120	..	...	..	2		
	9/ 4	6	..	33	..	...	..	1		
33	9/ 4	4	..	540	8	84	8	3		
	9/ 6	6	..	80	..	...	..	2		
34	9/ 5	5	..	77	2	86	12	2		
	9/10	10	..	46	10	90	0	1		
35	9/ 9	1	16	137	36	60	4	1	72	695
	9/16	8	4	5	..	...	..	1		
36	9/13	1	16	260	80	20	0	1		
37	9/16	1	..	90	10	78	12	1		

As shown by the chart, an increase in the number of cells occurred in the spinal fluid long after the disappearance of any discernible clinical evidence of the disease. Thus, in case 1 a count of 150 cells was obtained on the tenth day after the onset of the symptoms and a count of 17 cells on the nineteenth day, although the child was apparently normal on the fourth day. In case 6 a count showed 360 cells on the twelfth day after the onset, although the patient was normal clinically, except for an occasional headache, on the fifth day; in case 10 a count showed 150 cells on the ninth day after the onset, although the patient was apparently normal on the third day.

There was no significant increase in blood pressure; the content of chlorides and that of sugar were unaltered. In case 27 there was a value for carbohydrate of 134 mg. per hundred cubic centimeters in one examination, which could not be explained. Levinson and tryptophan tests were performed on four patients, with negative results; and examination for urea gave normal results. Two cultures of spinal fluid were sterile.

Blood counts were taken in twenty-four cases; they gave no characteristic results. The total white cell count was usually normal or reduced. It seemed possible that a low total count was more likely to occur in the early stages of the disease, although a low count was obtained in some cases for six or seven days after the onset. However, of fourteen counts made within four days of the estimated onset, eleven were below 10,000, while of eleven counts made four days after the estimated onset, only five were below 10,000 cells. There was no evidence of anemia. The Schilling index (of nineteen patients) indicated a mild infection, with no particular response of the blood. There were no stippled cells, characteristic of lead poisoning.

No information of value was obtained from other laboratory examinations. The urine of thirty-four patients was normal, with two exceptions. On culture the stool (six cases) gave no evidence of an abnormal condition; culture of material from the nose and throat gave negative results. Cultures of the blood (five cases) gave negative results. A Wassermann test of the spinal fluid in four cases gave negative results One test for sedimentation time gave negative results.

BACTERIOLOGIC DATA

Material from patients in the acute stage of the disease and later convalescent serums were subjected to study by Dr. Charles F. Church, of the Children's Hospital, Philadelphia, Dr. T. F. McNair Scott, of the Rockefeller Institute, New York, and Dr. Charles Armstrong, of the National Institute of Health, Washington.

An attempt was made to reproduce the disease in experiment on animals by intracerebral and intraperitoneal inoculations of spinal fluid,

blood serum and nasal washings obtained from patients in the acute stage of the disease and of suspensions made from the brain and spinal cord of the patient who died. All these workers reported that the material was not infectious for guinea-pigs, mice, rabbits or monkeys and that they were unable to reproduce any disease resembling acute choriomeningitis, anterior poliomyelitis or acute encephalitis either clinically or pathologically.

Dr. Scott and Dr. Armstrong used convalescent serum obtained from our patients in neutralization tests against known viruses. They reported that the convalescent serums afforded no protection against the virus of acute choriomeningitis. Dr. Scott further reported that negative results were obtained in neutralization tests against the virus of acute encephalitis of the type isolated during the St. Louis epidemic and the virus of poliomyelitis of the type obtained during the Philadelphia epidemic in 1931, as well as against mixed virus of poliomyelitis.

Table 5 shows the number of cases in which specimens were examined by these workers in each part of their study and the number of various experimental animals used.

REPORT OF CASE OF PATIENT WHO DIED

CASE 24.—A Negro girl 2 years of age was admitted to the hospital on the night of Aug. 24, 1935, and died on the following afternoon.[1] Three hours before admission she vomited, had several loose stools and shortly after had continuous generalized convulsions. The temperature was 106.5 F. She was comatose when admitted. General physical examination gave negative results. The Kernig sign was positive. The patellar reflex was hypo-active, and the abdominal reflexes were depressed. The biceps and triceps reflexes were present; the Babinski and Brudzinski signs were absent. Coma continued until the time of death. The spinal fluid was under 14 mm. of pressure and yielded 92 cells and a chloride content of 675 mg. per hundred cubic centimeters. Bacillus Watareka was cultured from the stool.[1]

Anatomic Diagnosis.—The diagnosis on the basis of anatomic observations was as follows: acute passive congestion and hyperplasia of the lymph nodes and thymus. The heart showed evidence of myocardial degeneration; the lungs, of acute passive congestion, with slight edema; the spleen, of follicular hyperplasia; the colon, of subacute hyperplastic colitis; the liver, of parenchymatous degeneration.

Pathologic Changes.—At autopsy the brain and cord showed intense edema and congestion, with gross evidence of diapedesis of red cells into the subarachnoid space.

Microscopic examination revealed degenerative changes in the endothelial cells of the capillary bed and evidence of generalized stasis, with resulting perivascular and pericellular edema.

1. This patient was admitted late on Saturday night and died the following afternoon (Sunday). An incomplete examination was made of the spinal fluid obtained in the receiving ward, and no further fluid was withdrawn before death.

TABLE 5.—*Summary of Experimentation on Animals*

Bacteriologist		Patients Examined for			Number of Animals Used			
		Chorio-meningitis	Polio-myelitis	Encephalitis	Monkeys	Mice	Guinea-Pigs	Rabbits
Scott.....	Acute*†	6	6	6	5	109	6	5
	Convalescent‡	9	1	5	2	..	?	..
Armstrong	Acute*	5	5	5	8	24	..	..
	Convalescent§	4	..	..	..	48	..	..
Church....	Acute*†	10	..	10	1	36	..	..
	Convalescent	..	..	..	..	..	..	..

* Spinal fluid, blood serum and nasal washings injected intracerebrally.

† Suspensions made from brain and spinal cord of patient who died injected intracerebrally and intraperitoneally.

‡ Neutralization tests with 1:10, 1:100 and 1:1,000 dilutions of choriomeningitis virus with convalescent serum.

§ Neutralization tests with 1:1,000, 1:6,666 and 1:33,333 dilutions of choriomeningitis virus with convalescent serum.

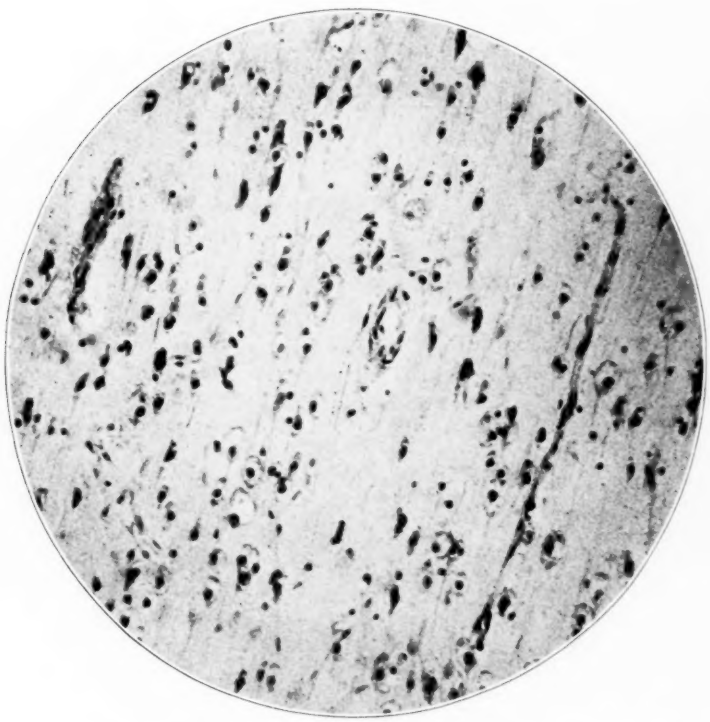

Fig. 1.—Photomicrograph of a section from the cortex, showing swelling of capillary endothelium, perivascular and pericellular edema and swelling and vacuolation of ganglion cells as well as ischemic and sclerotic cell degeneration (× 127).

In the cortex the ganglion cells showed extreme swelling of the cytoplasm, often with rupture of the cell membrane and detachment of the processes; ischemic degeneration was also noted. There was little or no reaction of the neuroglia cells except mild satellitosis. Similar changes were observed throughout the brain, but cellular degeneration was most severe in the vegetative nuclei of the tuber cinereum and medulla, in the Purkinje cells of the cerebellum and in the second and third layers of the cortex. There was evidence of perivascular hemorrhage in the periventricular gray matter of the third ventricle. A mild and sparse perivascular infiltration of lymphocytes and mast cells was noted, limited

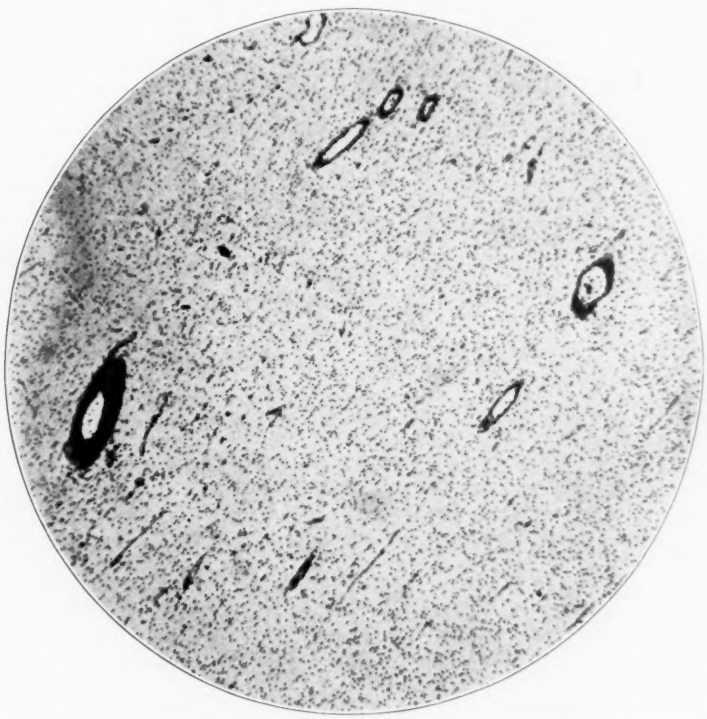

Fig. 2.—Photomicrograph of a section from the cornu ammonis, showing infiltration of lymphocytes and mast cells in the perivascular spaces; this area represents the maximum intensity of the infiltration (× 38).

entirely to the white matter. The most intense perivascular cuffing occurred in the cornu ammonis.

The spinal cord showed a thickened and hyalinized dura, with proliferation of the arachnoid around the nerve roots. The cord itself was edematous and showed peripheral demyelinization and ischemic degeneration in the anterior horn cells. Changes in the vessels were similar to those in the spinal cord. There was no evidence of perivascular infiltration or glial reaction. A diagnosis of acute encephalitis was made, although the degenerative changes in the ganglion cells and vascular apparatus suggested that the term "toxic degenerative state," as used in the German literature, might be sounder nomenclature. We hesitated to

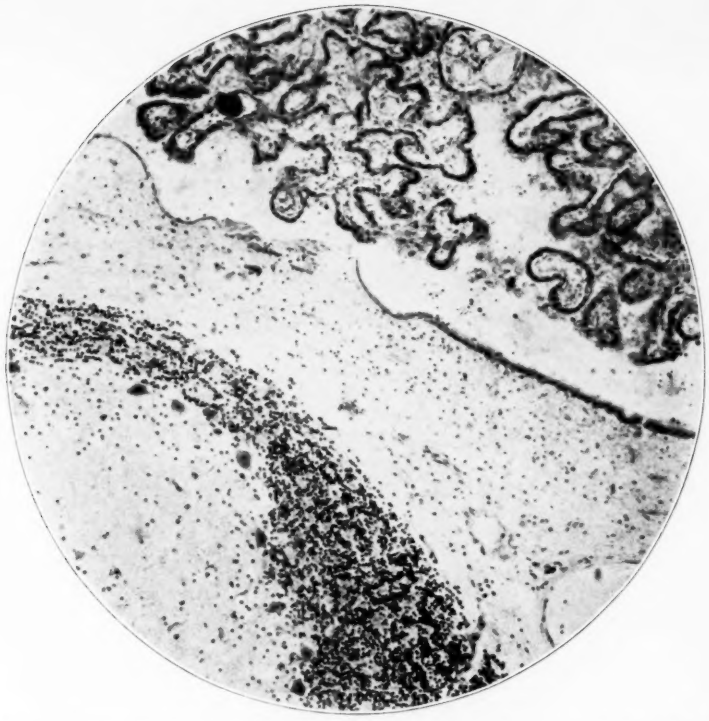

Fig. 3.—Photomicrograph of a section from the cerebellum and choroid plexus of the fourth ventricle, showing edema of the choroid with degeneration and desquamation of the epithelial cells, proliferation of the ependyma, loss of cells of the granular layer of the cerebellum and degenerative changes in the Purkinje cells, with proliferation of the Bergmann layer (× 80).

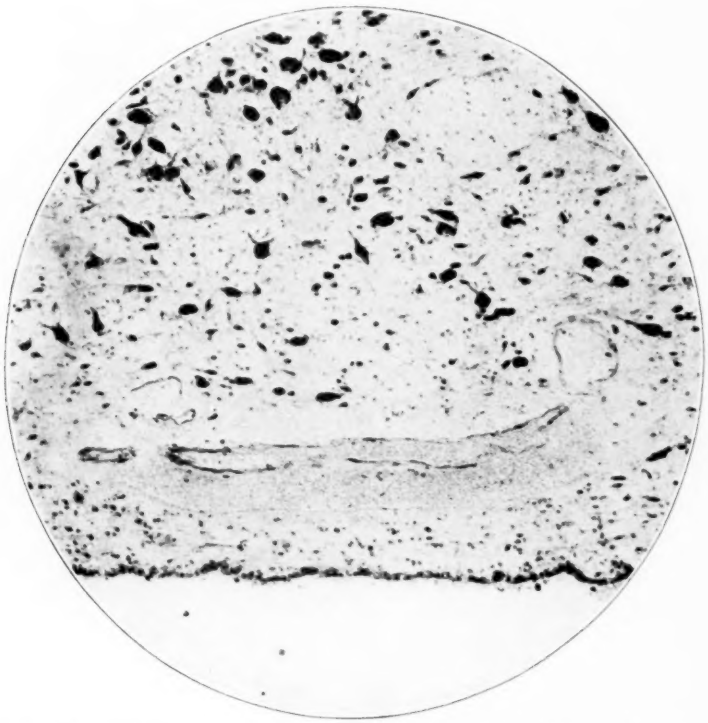

Fig. 4.—Photomicrograph of the paraventricular nucleus of the tuber cinereum, with perivascular hemorrhage around a dilated capillary, showing lysis of the wall. Degenerative changes in the hyperchromatic cells of the vegetative nucleus and ependymal proliferation and subependymal gliosis are present.

include this case in the series until we saw the slides from the case of the patient who died during the epidemic at Windber, Pa. They showed cerebral changes strikingly similar to those described in this paper. Communication with Dr. H. A. Slessinger, of the Windber Hospital, revealed that his patient had been ill for less than twenty-four hours and that two other members of the same family had been ill at the same time but had recovered.

From this information we concluded that the condition in our case was fulminant epidemic meningo-encephalitis. This supposition was strengthened by the observation of sequelae that pointed to organic disturbances in the central nervous system of twelve children less than six months after the onset of the acute disease.

COMMENT

That the condition was not poliomyelitis seems demonstrated by the following fact, that in consecutive cases thirty-seven children and twenty-six adults contracted the disease, without paralysis, and by the degree of familial incidence, and failure to produce poliomyelitis in animals by inoculation or to neutralize with convalescent serum the virus obtained during the epidemic in Philadelphia in 1931, or the mixed virus.

The condition in these cases was not acute choriomeningitis. The disease could not be reproduced in animals, and the convalescent serum afforded no protection against the virus.

Neutralization tests against the virus isolated during the epidemic of acute encephalitis in St. Louis gave negative results.

SUMMARY

A report is made of thirty-seven cases in which involvement of the central nervous system seems to have occurred. The pathologic changes in the nervous system of the patient who died are described. The nature of the condition was not determined, but apparently it was not due to bacterial invasion.

Case Reports

BRONCHIECTASIS AS A COMPLICATING CAUSE OF ASTHMA

ROBERT CHOBOT, M.D.
NEW YORK

The infrequency of bronchiectasis as a cause of asthma prompts me to report this case. A search of the literature does not reveal any report of a case of asthma caused by bronchiectasis in a child, though the studies on bronchiectasis are numerous. Thomson [1] in 1914 suggested that persistent bronchorrhea might be due to chronic suppuration in the lung; L. W. Dean [2] noted sinusitis in all his cases of bronchiectasis; Hodge [3] reported on a series of thirty-seven patients with bronchiectasis, 75 per cent of whom had sinusitis.

Bronchiectasis has been well described as a disease of childhood, and Singer and Graham [4] were the first to describe a triangular shadow at the base of the lungs in roentgenograms of children. Warner and Graham [5] demonstrated, from observations of bronchiectatic lobes both during operation and after their removal, that bronchiectasis may occur without the presence of either fibrosis of the lung or pleural adhesions. Anspach [6] reported fifty cases of bronchiectasis. He found that when the triangular shadow fluctuated in size and density from one examination to the next only tubular bronchiectasis developed, or the chest cleared up with little or no evidence of dilatation of the bronchi. When drainage did not occur with frequent reexpansion of the lobe or lobules, saccular bronchiectasis resulted. The latter condition developed in the

From the Allergy Clinic of the Department of Pediatrics, New York Post-Graduate Medical School and Hospital.

1. Thomson, St. Clair: Some of the Symptoms of the Complications of Sinusitis, Practitioner **92**:745 (June) 1914.

2. Dean, L. W.: Fundamental Things Influencing the Infection of the Nasal Sinuses, Ears and Lungs, Tr. Am. Acad. Ophth. **38**:225, 1933.

3. Hodge, G. E.: Relation of Bronchiectasis to Infection of Paranasal Sinuses, Arch. Otolaryng. **22**:537 (Nov.) 1935.

4. Singer, J. J., and Graham, E. A.: Roentgen Ray Study of Bronchiectasis, Am. J. Roentgenol. **15**:54, 1926.

5. Warner, W. P., and Graham, D.: Lobar Atelectasis as a Cause of Triangular Roentgen Shadows in Bronchiectasis, Arch. Int. Med. **52**:888 (Dec.) 1933.

6. Anspach, W. E.: Atelectasis and Bronchiectasis in Children, Am. J. Dis. Child. **47**:1011 (May) 1934.

finer, more distal bronchi, in which the thick secretion easily produced complete obstruction. Anspach expressed the opinion that allergy may aid in bringing about the initial obstruction by producing swelling of the mucous membrane and a thick, tenacious secretion.

I am reporting the following case, first, because of the rarity of bronchiectasis in asthmatic children and, second, because the bronchi eventually became the chief cause of the asthmatic paroxysms.

REPORT OF A CASE

History.—A boy 8 years of age was admitted to the allergy clinic of the pediatric department of the New York Post-Graduate Medical School and Hospital on Sept. 5, 1933, for treatment of asthma.

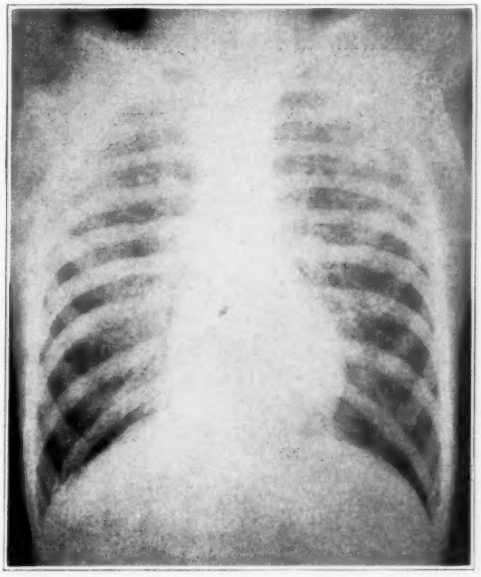

Fig. 1.—Roentgenogram taken Nov. 14, 1933, showing no evidence of bronchiectasis.

For the past four years he had been suffering from bronchial asthma. His attacks had been severe and without seasonal variation. During infancy he had facial eczema, which was made worse by his drinking milk and eating eggs; the eczematous condition disappeared at the age of 4 years. His past illnesses included chickenpox, measles and pertussis. His mother had severe eczema during childhood but did not have asthma; his paternal grandmother had asthma, and one cousin had hay fever.

Examination.—The child looked chronically ill and had beginning emphysematous changes in the chest. There was no evidence of clubbing of the fingers. Examination of the nose revealed an infection on the right side. The tonsils had been removed. At the time of the patient's admission the chest was filled with sonorous and sibilant râles. On Dec. 14, 1933, he had undergone an intranasal

antrotomy on the right side, adenectomy and partial removal of the right middle turbinate bone. Complete cutaneous testing was done, with negative results. Roentgen examination of the sinuses showed an involvement of the antrum and of the right ethmoid. Roentgen examination of the chest did not reveal a triangular shadow at the base, and the picture was considered typical of bronchial asthma.

Treatment and Course.—Elimination diets were attempted, with no positive results, and vaccine therapy as well as local treatments to the nose were instituted. During the year 1934 the nasal condition improved until it was considered no longer to be a factor in causing his attacks, which continued without abatement for a long time.

On Feb. 7, 1935, after a particularly severe attack of asthma, the sinuses and chest were again examined roentgenologically. The report of the examination of the sinuses was as follows: "The general structure is normal. The right antrum is moderately clouded. The right ethmoid sinus is moderately clouded; the

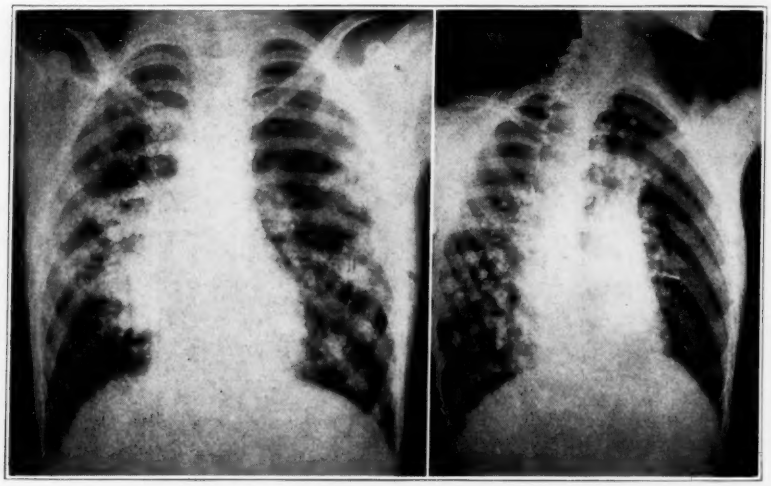

Fig. 2.—Roentgenograms taken May 10, 1935, after bronchoscopy with injection of iodized poppy-seed oil 40 per cent, showing bronchiectatic involvement most marked on the right side.

frontal and sphenoid sinuses are clear. The conclusion is that there is moderate membranous infiltration of the right antrum and the ethmoid sinus." The report of roentgen examination of the chest was as follows: "There is an anomalous development in that a small ossification center of a rudimentary rib is observed on the left with a supernumerary rib fully 1½ inches (3.8 cm.) in length on the right, developing from the last cervical vertebra. The transverse diameter of the heart is relatively small; its axis tends toward the vertical, corresponding to the elongated thorax. Otherwise no gross abnormality in the contour of the heart is demonstrable. There is a moderate degree of lymphoid nodulation at the hilus, with slight secondary root branch and central bronchial thickening. Though this is responsible for the accentuation of the pulmonic markings, there is no evidence of recent parenchymal infiltration or pleural involvement except a slight thicken-

ing in the upper septum on the right. The conclusion is: enteroptotic or hyposthenic status; moderate hilus and root branch thickening; anomalous rudimentary ribs in the upper part of the thoracic cage."

The patient's condition at that time became so bad that bronchoscopy was decided on. Examination of the urine gave negative results. Examination of the blood revealed: erythrocytes 5,140,000, leukocytes 8,400, hemoglobin 102 per cent (14.79 Gm. per hundred cubic centimeters) and color index 1. A differential count of 100 white cells showed: polymorphonuclear neutrophils 46 per cent, polymorphonuclear eosinophils 6 per cent, monocytes 2 per cent, small lymphocytes 23 per cent and large lymphocytes 13 per cent.

Dr. L. T. Perrault performed a bronchoscopy on the patient on February 9 and found the following condition: In the right bronchus the mucous membrane was red; a good deal of thick mucus came from the middle lobe. When iodized

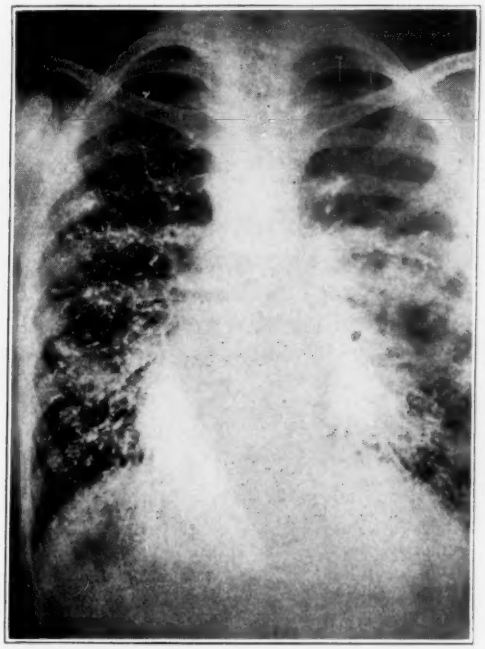

Fig. 3.—Roentgenogram taken July 23, 1935, showing beginning involvement of the left lung.

poppy-seed oil 40 per cent was first introduced, there seemed to be an obstruction; later an opening allowed some of the iodized oil to penetrate into the inferior lobe. In the left bronchus mucosecretion was found; no obstruction was observed. When the iodized oil was introduced it ran steadily into the inferior lobe. Reexamination and treatment were advised because of the apparent obstruction at the mouth of the bronchus of the inferior lobe.

A fluoroscopic examination at the time of the bronchoscopy, with the injection of iodized oil, revealed a large cavity, of irregular contour, about 4 cm. in vertical diameter and 2 cm. in width; the cavity was located posteriorly, close to the bronchus of the lower lobe. Injection of the oil into the lower lobe revealed a

confluent sacculated area low in the posterior costophrenic sinus. A bacteriologic examination of the fluid aspirated at the time of the bronchoscopy showed hemolytic streptococci in the fluid, which otherwise was normal except for a few pus and epithelial cells.

After the bronchoscopy the patient showed marked improvement so that for the first time in weeks the use of epinephrine was discontinued. Since then at three to four week intervals a bronchoscopy has been performed; each time fluid has been aspirated from both cavities. Both his general condition and his asthmatic condition have improved. His attacks are now about half as severe as they were and usually reach their peak just before the bronchoscopy is performed; after each bronchoscopy there is a temporary improvement.

COMMENT

This case illustrates the fact that bronchiectasis can be present without evidence of a triangular shadow at the base of the lungs. The presence of a bronchiectatic cavity unrevealed by ordinary procedure again emphasizes the importance of injections of iodized oil. It is unusual that a bronchial infection, which undoubtedly originated in the patient's sinuses, became the chief cause of his asthma. It is interesting to observe that emptying the cavity causes a lessening in the severity of the attacks and an improvement in the patient's general condition. I have found, however, that after three weeks the attacks begin to resume their severity and bronchoscopy must be resorted to. Whether this type of therapy will continue to be effective I cannot yet tell, but great care is being taken to build up the child's general resistance.

SUMMARY

A case of infective asthma in a child 8 years old is reported.

An unusual feature is the fact that bronchiectasis developed despite therapy directed to the initial focus of infection in the nose and remained undiagnosed until iodized oil was injected.

The asthma became controllable when the bronchiectatic cavity was emptied. The treatment for the past year, which has consisted only in repeated bronchoscopic treatments, has resulted in a definite improvement in the general health of the patient.

30 West Fifty-Ninth Street.

USE OF A PENTAVALENT ANTIMONY COMPOUND FOR TREATING KALA-AZAR IN CHILDREN

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TSINAN, CHINA

This report is concerned with presenting in detail the routine administration of a pentavalent antimony compound [1] for treating a child with kala-azar, and with reviewing the therapeutic value of this drug in treating kala-azar in children of North China.

REPORT OF A CASE

M. W. Ch'en, a Chinese boy aged 9 years, came from a village in a region where kala-azar was endemic. He had been healthy until fifteen months before admission, when his father noticed that the child was gradually becoming listless. For nine months before admission he had frequent irregular attacks of fever. Since the onset of the present illness there had been gradual loss of appetite, strength and weight and frequent attacks of bleeding from the nose and gums. A mass reaching 2 fingerbreadths below the left costal margin was noticed in the upper part of the abdomen eight months before admission. This mass had gradually enlarged downward. One month before admission the patient began to pass three or four loose stools daily, but no blood or pus was noticed in the stools.

The past history indicated nothing remarkable. He was vaccinated against smallpox at the age of 2 years. At 6 years multiple abscesses developed in the skin over the abdomen, scalp and right knee. At 8 years he had measles. For several years he had complained of mild irregular attacks of generalized abdominal pain. The feeding history showed that the child had taken no milk since he had been weaned from the breast. He rarely took eggs or meat. The daily diet consisted of steamed bread, cabbage, spinach, carrots and sweet potato when these were in season.

Both parents and one younger brother were living and well. A sister died of measles at 6 years of age. Two years before the admission of the patient another sister, 6 years of age, died as a result of a mass in the abdomen, which was accompanied by necrosis of the mouth. During this illness the sister lived in the home with the patient. The parents said that the sister died of a disease similar to the illness presented by the patient.

There were about one hundred and seventy families in the patient's home village. Six children in these families were known to be suffering from a disease similar to the illness presented by the patient. A relative from the same village

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1. The compound used was the para-aminophenylstibinate of diethylamine, which contains about 40 per cent antimony in the pentavalent form. It is manufactured by Bayer-Meister Lucius, Leverkusen, Germany.

was treated for kala-azar in the Cheeloo University Hospital a year before the patient was seen and was well at the time of the patient's admission.

Physical examination revealed an undernourished and listless boy, lying in bed. The mucous membranes were pale, and there was profuse sweating of the head.

TABLE 1.—*Patient's Condition at Beginning, Middle and End of Treatment with a Pentavalent Antimony Compound*

	Admission, May 4	May 11 or 12	May 16 or 17
Appearance	Weak, pale, listless	Interested	Active, happy
Temperature, C.	38.6	38.1	37
Body weight, Kg.	19.6	17.61	
Size of liver, cm.	5	5	5
Size of spleen, cm.	15	13	13
Hemoglobin content, Gm.	6.3	8.1	8.5
Red cell count	2,080,000	3,058,000	3,510,000
White cell count	2,100	2,800	2,780
Polymorphonuclears, percentage	36	42	45
Large monocytes, percentage	4	4	2
Blood platelets	150,000	160,000	158,000
Globulin-albumin ratio of blood serum		4.9-2.8	
Serum globulin reaction	Positive	Test not made	Positive
Serum calcium content, mg. per 100 cc.		6.9	
Widal reaction	Negative	3 injections of triple typhoid vaccine given	Positive for B. typhosis with a 1:320 dilution; positive for B. paratyphosis B with a 1:320 dil.
Bleeding time, minutes	15	Not determined	6
Coagulation time, minutes	16	Not determined	13
Cultures made following splenic puncture	Leishmania observed 11 injections of the antimony compound given (with a total of 2.1 Gm.)	.....	Leishmania not observed
Nasal smears	Leishmania not observed		
Sedimentation rate	17.3		16.75
Smear from gums	Vincent's spirochete observed		
Smear of stool	Ova of Ascaris observed 3 grains (0.18 Gm.) of santonin given	.....	Not observed
Urine	Normal	Normal	Normal
Mantoux reaction	Negative with 0.1 mg. of tuberculin	Negative with 1 mg. of tuberculin	
Schick reaction	Positive	1 cc. of alum-precipitated diphtheria toxoid given	

The temperature was 38.6 C. (101.5 F.); the height was 44 inches (111.7 cm.); the head measured 20½ inches (52 cm.); the chest, 24½ inches (62.2 cm.), and the abdomen, 23 inches (58.4 cm.). The weight was 19.6 Kg. The skin was pale. There were one large scar over the left parietal region, three over the right side of the abdomen and two over the right thigh. The conjunctivae were pale and

contained many granules. The gums were swollen and pale, and pressure on them produced a purulent discharge around the teeth. The tonsils and the cervical and inguinal glands were slightly enlarged. The lungs were clear. The heart was normal in size and position; a soft systolic murmur over the base was not transmitted beyond the precordium. The abdomen was soft and distended. The liver was 5 cm. below the costal margin in the right nipple line. The spleen reached 15 cm. below the costal margin in the left nipple line. The extremities were emaciated; there was no edema. All the deep reflexes were normal. The Chvostek and Trousseau signs were not elicited.

Leishman-Donovan bodies were seen in material taken by splenic puncture at the time of admission, and the intravenous injection of a pentavalent antimony compound was started the following day. A fresh solution was used; the drug was dissolved in distilled sterile water to make a 5 per cent solution. The first injection contained 0.1 Gm. of the antimony compound as the patient showed no reaction, 0.2 Gm. was injected daily until a total dose of 2.1 Gm. was given. The tempera-

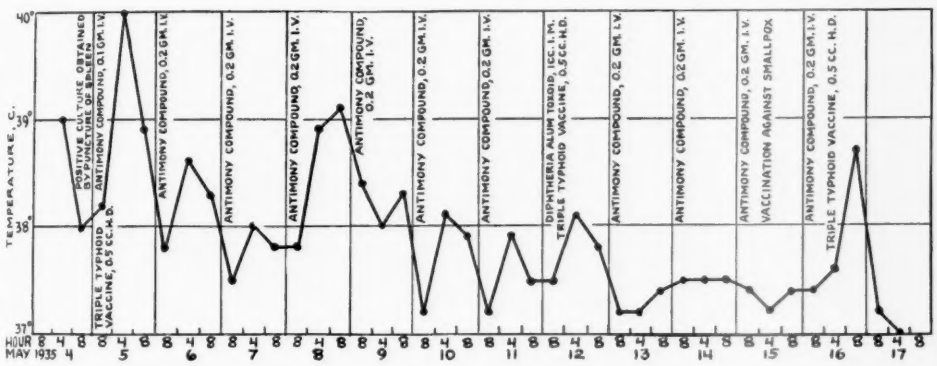

Chart showing the temperature curve of the patient during the course of treatment. *H.D.* indicates hypodermically; *I.V.*, intravenously, and *I.M.*, intramuscularly.

ture remained below 38 C. (100.4 F.) after the patient had received 1.1 Gm. of the antimony compound. Kala-azar was considered the primary etiologic factor in the anemia, which, in addition to treatment for kala-azar, was treated with a 10 per cent solution of iron and ammonium citrate, given daily by mouth in doses of 2 cc. per kilogram of body weight, and with a 0.5 per cent solution of copper sulfate, given daily by mouth in doses of 0.5 cc. per kilogram of body weight. The child ate heartily the regular diet for children with kala-azar which, in addition to cereal and vegetables, contained 6 ounces (170 Gm.) of liver and 1 quart (946 cc.) of milk daily. Three grains (0.18 Gm.) of santonin was given on the fifth day in the hospital; after this the patient passed ten Ascarides, after which he did not complain of abdominal pain. A 1:2,000 solution of zinc chloride was used as a mouth wash after meals, three times daily. A 0.5 per cent solution of copper sulfate was used for eye drops three times daily.

RESULTS OBTAINED FROM TREATING TWO HUNDRED AND FORTY-THREE CHILDREN WITH PENTAVALENT ANTIMONY COMPOUND

Between October 1928 and December 1934, 243 children suffering from kala-azar were treated with the pentavalent antimony compound under consideration. These children were treated in the pediatric service of the Cheeloo University Hospital. They had received no treatment with antimony before admission. Eight of the number died in the hospital before the course of treatment was finished. Two hundred and thirty-five children received a full course of the antimony compound and were discharged home. In March 1935 a questionnaire was sent

TABLE 2.—*Survey of Results of Treatment of 233 Children with Kala-Azar Who Had Received a Full Course of a Pentavalent Antimony Compound*

No reply	97	Previous survey showed kala-azar cured	27
Letter undelivered	32		94
Replied that kala-azar was cured	94		2
Returned for examination; kala-azar cured	2		4
Visit to home; kala-azar cured	4		
Died	3		
Kala-azar not yet cured	1		
Treated	233	Reported cured	127

TABLE 3.—*Period When Patient Was Reported Cured of Kala-Azar After End of Treatment with a Pentavalent Antimony Compound*

Number of Patients	Time from Discharge to Date of Report
19	1-6 mo.
20	6 mo-1 yr.
19	1-2 yr.
20	2-3 yr.
31	3-4 yr.
11	4-5 yr.
11	5-6 yr.

to the homes of 233 of the children who had received a full course. Table 2 shows the results of this survey.

COMMENT

The introduction of pentavalent organic antimony compounds for the treatment of kala-azar is undoubtedly an advance in chemotherapy. From the results obtained with treating a limited number of children suffering from kala-azar with one such compound, I feel that it is the antimony preparation which has given the best results in the patients under the observation of my colleagues and me. In most cases the course can be finished in two weeks. A review of patients treated in the clinic and hospital of Cheeloo University since October 1928 shows that for children without noma the mortality rate is 1.5 per cent and

for patients with kala-azar complicated with noma it is below 16 per cent.[2] During the spring of 1935, letters were sent to all the patients who had received treatment with the pentavalent antimony compound for kala-azar. Patients who lived near enough to be visited were seen at home. Table 2 gives the details of the results of this survey of treated patients.

Briefly, of 235 patients discharged alive, satisfactory reports were received for 127 from one month to seven years following completion of the treatment. Of this number, 96.9 per cent gave evidence indicating cure of kala-azar.

2. Fan, P. L., and Scott, Annie V.: A Study of Noma Complicating Kala-Azar in Children, Chinese M. J. **48**:1046 (Oct.) 1934.

DUODENITIS

I. R. JANKELSON, M.D.

BOSTON

Judd [1] is universally given credit for first recognizing duodenitis as an operative and pathologic entity. The findings at operation were described by him as hyperemia and stippling of the serosa of the duodenal bulb. There is little infiltration; so the thickness of the duodenal wall appears normal or only slightly increased. When the duodenal cap is opened, the mucosa appears unbroken, is either diffusely or locally inflamed, bleeds easily on manipulation and on close inspection may present one or more small, superficial fissures or ulcerations. The microscopic changes were described in this country by MacCarty [2] and Wellbrock.[3] They are characterized by a thickening of the mucosa and submucosa due to edema and congestion and by infiltration with polymorphonuclear leukocytes, lymphocytes, plasma cells and endothelial leukocytes. There are some cellular destruction and denudation. The epithelial cells may present various stages of degeneration. The serosa is usually only slightly thickened. The blood vessels are moderately sclerosed but not obliterated. In the cases of more chronic involvement there is more fibrous tissue throughout the coats of the duodenal wall and fewer polymorphonuclear leukocytes. Konjetzny [4] described similar gross and microscopic appearances in duodenitis both in the presence of a duodenal ulcer and in its absence. He stated the belief that a chronic duodenal ulcer develops on the base of a chronic duodenitis. Nagel,[5] Wellbrock,[3] Faber [6] and the Kelloggs [7] agreed with this point of view

1. Judd, E. S.: Pathologic Conditions of Duodenum, Journal-Lancet **41**:215 (April) 1921.

2. MacCarty, W. C.: Excised Duodenal Ulcers, J. A. M. A. **83**:1894 (Dec. 13) 1924.

3. Wellbrock, W. L. A.: Duodenitis and Duodenal Ulcer, Ann. Surg. **91**:533 (April) 1930.

4. Konjetzny, G. E.: Gastritis, Duodenitis und Jejunitis in ihrer Bedeutung für den Chirurgen, Beitr. z. klin. Chir. **152**:552, 1931.

5. Nagel, G. W.: Duodenitis, in Collected Papers of the Mayo Clinic and the Mayo Foundation, Philadelphia, W. B. Saunders Company, 1926, vol. 18, p. 153.

6. Faber, K.: Pyloric Symptom Complex, Acta med. Scandinav. **26**:358, 1928.

7. Kellogg, E. L., and Kellogg, W. A.: Duodenitis, Am. J. Surg. **21**:368 (Sept.) 1933.

but presented no proofs for their contention. On the other hand, Judd,[1] Hauser,[8] Buchner and Knotzke[9] and Radecke[10] denied any interrelationship between duodenitis and duodenal ulcer. Aschner and Grossman[11] demonstrated that duodenitis accompanies a duodenal ulcer and probably is the cause of repeated recurrences of ulcer activity.

The clinical manifestations of duodenitis in a general way resemble those of a duodenal ulcer. Pain, if present, is likely to be diffusely distributed throughout the upper part of the abdomen and may radiate into the back or chest. This pain is gnawing or burning but rarely sharp. It is often related to the intake of food and reaches maximum severity from one to three hours after meals. Alkalis relieve the pain to a lesser degree in cases of duodenitis than in those of duodenal ulcer. In about 20 per cent of the cases there is no pain. Rivers,[12] who analyzed seventy-four cases of duodenitis without an accompanying ulcer, stated that in 35 per cent the symptoms did not resemble those of a duodenal ulcer. Lipschutz,[13] who reported ten cases, and Miller,[14] who studied twenty-six cases, expressed the opinion that the symptoms of duodenitis and those of duodenal ulcer are identical. Hufford[15] stated that the symptoms of duodenitis are the less severe. Fulness and distress, soon or several hours after meals, may be the only complaint. Nausea, belching and heartburn are common. Vomiting occurs rarely in this condition. Hemorrhage, both gross and occult is common; it may be the first and only symptom. In the cases discussed by Rivers,[12] 12 per cent of the patients had gross hemorrhages at one time or another. Pyloric obstruction seemingly does not occur. Perforation of the duodenum has not been reported in association with duodenitis without an accompanying ulcer. Johnson,[16] who studied the gastric contents of seventy-seven patients with duodenitis, found normal secre-

8. Hauser, G.: Ueber die Beziehungen der chronischen Gastritis und Duodenitis zum chronischen Magen- und Duodenalgeschwür, Med. Klin. **23**:120 (Jan.) 1927.

9. Buchner, F., and Knotzke, F.: Ueber akute peptische Duodenitis, Beitr. z. path. Anat. u. z. allg. Path. **80**:496 (March) 1928.

10. Radecke, H.: Ueber akute peptische Veränderungen des Duodenums, Beitr. z. path. Anat. u. z. allg. Path. **84**:617 (May) 1930.

11. Aschner, P. W., and Grossman, S.: Gastritis and Duodenitis in Relation to the Ulcer Problem, Surg., Gynec. & Obst. **57**:334 (Sept.) 1933.

12. Rivers, A. B.: Clinical Study of Duodenitis, Gastritis and Gastrojejunitis, Ann. Int. Med. **4**:1265 (April) 1931.

13. Lipschutz, E. W.: Subacute Recurrent Duodenitis, Internat. Clin. **4**:245 (Dec.) 1930.

14. Miller, T. G.: Duodenitis: Review of Twenty-Six Cases so Diagnosed, M. Clin. North America **14**:841 (Jan.) 1931.

15. Hufford, A. R.: Duodenitis, J. Michigan M. Soc. **30**:267 (April) 1931.

16. Johnson, T.: Chronic Duodenitis, South. M. J. **21**:1031 (Dec.) 1928.

tion in thirty, hypersecretion in twenty-five and hyposecretion in twenty-two cases. Judd reported that there is usually a high acid content, while Kellogg reported one case in which anacidity occurred after a test meal.

The most important evidence of the presence of duodenitis is obtained by roentgen examination. The roentgenologic picture was described by Kirklin [17] and Miller.[14] There is an inconstant deformity of the duodenal cap without a marginal niche or a central fleck. The duodenum is irritable; it fills indistinctly and empties rapidly. The bulb is usually small and grossly deformed, and the deformity varies quickly from moment to moment. The cap lacks density, and the margins may be hazy. The mucosal pattern is coarsely and irregularly reticular. The stomach frequently shows active peristalsis and increased tone. There is often transient pylorospasm, but the presence of gastric residue after six hours is rare.

The diagnosis of duodenitis is made mainly by exclusion. Duodenal ulcer and other lesions which may produce duodenal spasm or deformity both inside and outside the gastro-intestinal tract must be carefully excluded. The diagnosis may not be clear, and a period of close observation and repeated roentgenologic studies may be necessary to confirm or rule out a diagnosis of duodenitis. According to Eusterman and Balfour,[18] the diagnosis can never be made with certainty except by exploratory laparotomy and a pathologic study. However, several hundred cases of duodenitis without an accompanying ulcer have been reported. In some of these cases the diagnosis was confirmed by pathologic study; in others, it was made only on the basis of the clinical and roentgenologic manifestations. A perusal of the literature reveals no report of a case of duodenitis in childhood. Because of this I am reporting two cases observed recently.

REPORT OF CASES

CASE 1.—S. S., a 5 year old boy, was first seen in January 1934. At that time the chief complaint was persistent distress in the epigastrium of two and one-half years' duration; during the last six months there was also pain. Seemingly the pain was fairly sharp, as the boy was frequently awakened from sleep; at times he would cry out from a sound sleep. The pain was relieved by food and aggravated by hunger. There were some belching and a sensation of heat in the stomach. On one or two occasions there was vomiting; the vomitus smelled sour and consisted of recently eaten food. There was no projectile vomiting or hematemesis. The bowels moved daily without laxatives. There was a

17. Kirklin, B. R.: Duodenitis and Its Roentgenologic Characteristics, Am. J. Roentgenol. **31**:581 (May) 1934.

18. Eusterman, G. B., and Balfour, D. C.: The Stomach and Duodenum, Philadelphia, W. B. Saunders Company, 1935, p. 355.

normal gain in weight. The past history revealed a normal delivery and normal development. Up to the age of 8 months the patient had been breast fed. After that the diet was well balanced and sufficient. The patient had had repeated sore throat and infections of the upper respiratory tract, which resulted in chronic bilateral otitis media and in mastoiditis on the left, which required surgical intervention in May 1933.

The physical examination revealed nothing abnormal except the scar of the operation on the mastoid and discharge from both ears. The tonsils had been removed surgically. The heart and lungs were normal. The abdomen was soft and not tender; there were no masses, spasm or rigidity. The liver, spleen and kidneys were not palpable. Repeated examinations of the urine gave negative results. A cytologic study of the blood showed nothing abnormal. The gastric analysis after injection of histamine showed free hydrochloric acid 14 and total acidity 35; there was neither gross nor occult blood. Roentgen examination of the gastro-intestinal canal revealed the stomach to be in normal position, of regular outline and of normal size. The peristalsis was slightly increased, and the tone was normal. The duodenum was difficult to fill; the cap was somewhat irregular, but the irregularities were not characteristic of an ulcer. There was no gastric residue after six hours. The colon was normal. The appendix was visualized, freely movable and not tender.

No definite diagnosis was made at that time. With a soft solid diet and small doses of tincture of belladonna, the patient improved somewhat for approximately two months. Then there were a recurrence and an aggravation of the same symptoms. The patient showed a finicky taste and a fear of some foods. He lost 3 pounds (1.36 Kg.) in weight. The night distress became more frequent and was accompanied by a persistent demand for food, the boy insisting on crackers or cookies. In June of the same year another roentgen examination of the gastro-intestinal tract disclosed a typical ulcer deformity in the duodenum. There was no gastric residue after six hours.

On a diet for the relief of ulcer, with alkalis, the patient became free from symptoms in five days, and he remained so except for short exacerbations on two occasions caused by indiscretion of diet.

Diagnosis.—A diagnosis of duodenal ulcer was made. In retrospect, the evidence of the deformed duodenum shown by the first roentgen examination must be interpreted as duodenitis.

Case 2.—H. B., a 10 year old boy, was first seen in March 1934, complaining of epigastric distress and pain of four years' duration. When he was 6 years old, severe cramplike pain developed in the abdomen. The onset was acute, waking the patient from a sound sleep. The pain was accompanied by vomiting, and the mother believed that on one occasion the vomitus contained some blood. The patient continued to have some vague abdominal pain, coming at irregular intervals without any relationship to food. Rarely there was some vomiting, and if it occurred, it was usually late in the evening or during the night. He had lost 4 pounds (1.8 Kg.) in weight and appeared pale. Six weeks later a roentgen examination revealed a retrocecal appendix, which was somewhat tender. The symptoms persisted, and approximately three months later an appendectomy was performed. Following it, there was complete relief for about one year.

When the child was 7½ years old the symptoms recurred. At that time the pain was localized more in the upper part of the abdomen and occurred mainly at night. Rarely was the pain accompanied by vomiting. A roentgen examination

at that time showed a flattened, poorly filled duodenum with a nonpersistent deformity, interpreted as a spasm of the duodenum. The patient was placed on a bland diet and given belladonna. There were repeated remissions and exacerbations of his symptoms.

The physical examination revealed nothing abnormal except a right paramedian postoperative scar. The urine was normal. The red blood cells numbered 5,720,000; the hemoglobin content was 85 per cent; the white blood cells numbered 7,800. The gastric analysis after injection of histamine showed free acidity 18 and total acidity 32. There was persistent occult blood in the stools when the patient was on a meat-free and fish-free diet. Another roentgen examination showed a definite persistent deformity of the duodenal cap with hyperperistalsis of the stomach. There was no gastric residue after six hours.

A diagnosis of duodenal ulcer was made. On a Sippy regimen, with alkalis and rest in bed, the patient became symptom-free and remained so. In retrospect, the findings at the second roentgen examination in addition to the suggestive symptoms must be interpreted as duodenitis, which within one year developed into a duodenal ulcer.

COMMENT

In these two patients followed for almost two years, typical duodenal ulcer deformities developed while they were under observation. In both cases preceding the appearance of the ulcers, the duodenum was found to be irregular, poorly filled and deformed. In neither case was the diagnosis of duodenitis made. When the roentgenograms were reviewed definite evidence of pathologic changes within the duodenal cap could be found. Functional disturbances of the duodenum were suspected on the basis of the roentgen picture, but the further course of the disease made this diagnosis unlikely. Also, the possibility of a duodenal ulcer was ruled out by a careful fluoroscopic and roentgenographic examination at that time. Thus, both cases must be accepted as instances of duodenitis terminating in a duodenal ulcer.

In a previous contribution[19] I have pointed out that peptic ulcer is more common in children than is generally believed. In that article the possibility also was suggested that in many cases in which peptic ulcer was observed in an adult the condition originated in childhood but was not recognized at that time. The question may justly be raised whether unrecognized duodenitis in children may not eventually develop into duodenal ulcer in adult life. A plea should also be made for more roentgen studies of the gastro-intestinal canal in children who exhibit chronic or recurrent digestive symptoms. The recognition and proper treatment of duodenitis in childhood may be the best prophylaxis against the development of a duodenal ulcer in childhood or in adult life. I agree with the cited contributors who believe that

19. Jankelson, I. R.: Peptic Ulcers in Children, Am. J. Dis. Child. **44**:162 (July) 1932.

duodenitis not only accompanies a duodenal ulcer but frequently precedes it and is a predisposing factor in its formation. Nothing in this statement, however, should be construed as implying that duodenitis must terminate in a duodenal ulcer. On the contrary, some patients get well with or without treatment; in others the condition remains stationary, but in some it progresses to ulcer formation. I shall not consider here whether predisposition, constitutional factors, intercurrent infections, foci of infection and diet have any direct bearing on the course of duodenitis. The importance of early diagnosis and early treatment of ulcer disease (in this category duodenitis is included) is emphasized by the fact that experience has shown that the quicker the disease is properly treated, the better the immediate results and the fewer the complications. It is, however, worth while to be aware of the frequency of frank hemorrhage in duodenitis.

The diagnosis of duodenitis presents many difficulties and often may be questioned. It is well recognized that some ulcers, particularly those of the posterior wall, may be overlooked even by the most skilful fluoroscopist and roentgenologist. The tendency today is to make a diagnosis of a duodenal ulcer more frequently than in the past, but often it is made on doubtful or insufficient evidence. On the other hand, irritability and poor filling and rapid emptying of the duodenal cap may be caused reflexly by a distant lesion within the gastrointestinal tract or elsewhere in the body. The diagnostic difficulties are further increased by the frequent simultaneous occurrence of both duodenal ulcer and duodenitis, on which spasms may be superimposed. Repeated roentgen studies may be necessary in some cases to make a definite diagnosis. Without roentgen evidence duodenitis can be only suspected. A carefully planned dietetic regimen, carried out for from six to eight weeks or longer, followed by further roentgenologic observation may help to confirm the diagnosis. Exploration of the abdomen in cases of duodenitis for diagnostic purposes should not be necessary and should be avoided.

The treatment of duodenitis in children, as well as in adults, is the same as that of a duodenal ulcer. Rest, a carefully graded dietetic regimen, elimination of foci of infection and administration of alkalis in doses sufficient to neutralize the stomach contents but not large enough to produce alkalosis are the accepted factors in treatment. When a child is given a first stage Sippy diet, with its excessive fat content, ketone bodies frequently appear in the urine. Their presence, however, need not produce anxiety, for when the second stage diet, with its increased carbohydrate intake, is given the equilibrium is reestablished and ketogenesis disappears. Fortunately, perforations and serious delay in gastric emptying do not occur in cases of duodentitis not

accompanied by an ulcer. Hemorrhage occurs and may be serious. Surgical intervention, which has been resorted to altogether too frequently in treatment of this condition, is seldom justifiable.

CONCLUSIONS

Two cases of duodenitis in children are reported. These are the first cases of duodenitis in children to be reported. It is suggested that in the past duodenitis has been frequently overlooked and not properly treated. The best prophylactic measure for the control of a duodenal ulcer is the early recognition and proper treatment of duodenitis. The literature pertaining to duodenitis is reviewed. A plea is made for study by roentgen examination of the gastro-intestinal tracts of children who exhibit chronic or recurrent digestive symptoms.

BACTEREMIA DUE TO THE GRAVIS TYPE OF CORYNEBACTERIUM DIPHTHERIAE

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AND
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Clinical diphtheria is essentially an intoxication. The diphtheria bacillus is able, while growing superficially on the mucous membranes of the upper respiratory tract, to elaborate toxin, but only rarely does it invade the deeper tissues or blood stream. Zinsser and Bayne-Jones [1] expressed the opinion that although this organism had been isolated from the liver and spleen post mortem, the occurrence of septicemia due to the diphtheria bacillus during life had never been proved.

Andrewes and his associates,[2] however, in their report on diphtheria to the Medical Research Council, discussed the results obtained by a group of workers in Hamburg who studied the disease from 1909 to 1913 and concluded that there were 2 authentic cases of bacteremia due to pure Corynebacterium diphtheriae on record. Roedelius [3] succeeded in isolating diphtheria bacilli from the blood in pure culture from 2 patients in this series of cases. The positive cultures were obtained from 2 children, aged 9 and 5 years, respectively, who were critically ill and showed purpuric manifestations. In spite of the fact that culture of the blood of 1 of these patients was positive for diphtheria bacilli on the fourth day of the disease and that purpura developed on the seventh day, the patient made a gradual recovery and was discharged on the sixty-sixth day. Roedelius stated that among 1,000 patients with diphtheria observed at the Eppendorf Hospital in Hamburg from 1910 to 1912, this child was the only patient with purpuric manifestations who survived. It is also of interest that among the 187

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1. Zinsser, H., and Bayne-Jones, S.: A Textbook of Bacteriology, ed. 7, New York, D. Appleton-Century Company, Inc., 1934, p. 472.

2. Andrewes, F. W., and others: Diphtheria: Its Bacteriology, Pathology and Immunology, Medical Research Council, London, His Majesty's Stationery Office, 1923, pp. 226-229.

3. Roedelius, E.: Ueber das Vorkommen von Diphtheriebazillen im stromenden Blut, Ztschr. f. Hyg. u. Infektionskr. **75**:497, 1913.

cases of diphtheria carefully studied by Roedelius, cultures of the blood of 12 other patients with "hemorrhagic diathesis" were sterile during life.

In the series of 313 blood cultures made by the Hamburg workers, C. diphtheriae was isolated on one other occasion (Leede [4]), but in this instance it was present in combination with streptococci. The invasion of the blood by C. diphtheriae in Leede's case might be considered secondary to the streptococcic septicemia.

In view of the fact that septicemia due to the diphtheria bacillus is extremely rare, it seems of interest to report a case of severe diphtheria in which the blood culture was positive twenty-six hours before the patient's death. Furthermore, in view of the association noted by English workers of a certain type of diphtheria bacillus (gravis) with severe forms of diphtheria, a bacteriologic study of the organism isolated from this patient was made.

REPORT OF A CASE

A Chinese girl of 18 years was admitted to the hospital on Nov. 14, 1935, complaining of sore throat, pain on swallowing and fever of about one day's duration. The onset of the symptoms was sudden. She first noticed that her throat was sore on the morning of November 13, and toward evening she felt feverish. She was nauseated at times but did not vomit. Her past history was unimportant, except for the fact that she had had 3 attacks of urticaria, once every spring for three years, the last occurring about six years before admission. Her younger brother was admitted to the hospital on the day before the patient, with severe faucial diphtheria of five days' duration.

On admission the patient appeared to be fairly ill and uncomfortable. Her face was flushed but not cyanotic. The skin was clear, breathing was normal and the voice not hoarse. The anterior aspect of the neck was diffusely swollen, owing to the presence of enlarged and tender cervical and submaxillary lymph nodes. The lips were dry and the breath slightly foul. The throat was moderately injected, and both tonsils were greatly enlarged, meeting in the midline. A thin layer of yellowish and sanguineous membranous exudate covered the entire pharynx. Bleeding was easily produced by peeling off the exudate. The heart, lungs and abdomen were essentially normal. The blood pressure was 102 systolic and 60 diastolic.

The results of the laboratory examination were as follows: The red blood cells numbered 4,160,000 per cubic millimeter; the hemoglobin content was 12.4 Gm. per hundred cubic centimeters, and the white cells numbered 15,050 per cubic millimeter, with 78 per cent polymorphonuclear neutrophils. The urine contained a trace of albumin. A smear made from the material from the throat showed many morphologically typical Klebs-Löffler bacilli. This observation was confirmed by culture, and a small number of hemolytic streptococci were also present. On culture the material from the nose showed no diphtheria bacilli.

Course.—The patient showed a slightly positive reaction to horse serum by the intradermal test. Thirty thousand units of diphtheria antitoxin, produced by the National Epidemic Prevention Bureau at Peiping, was therefore given intra-

4. Leede, W.: Bakteriologische Blutbefunde bei Diphtherie, Ztschr. f. Hyg. u. Infektionskr. **69**:225-242, 1911.

muscularly by the desensitization method. The following morning the throat appeared to be necrotic and sloughing, and the patient felt more difficulty in swallowing and in breathing. She vomited some bloody material occasionally and looked extremely toxic. In view of the absence of improvement of the local as well as the general condition of the patient, another 20,000 units of diphtheria antitoxin was given intramuscularly, about twenty-four hours after the first dose. She seemed to show slight improvement during the next two days. The temperature, which on admission had been 40.5 C. (104.9 F.), came down gradually to 38.5 C. (101.3 F.). On the fifth day after admission, however, the temperature began to rise again, and her general condition became rapidly worse. She looked toxic and anxious. A few purpuric spots developed over the chest, back and arms. Each measured from about 2 to 4 mm. in diameter. The bleeding time was determined to be four minutes. Because of the possibility of streptococcic septicemia, blood was taken for culture at 9:30 a. m. on November 18. On the next day a growth of 34 colonies of C. diphtheriae per cubic centimeter of blood was obtained in pure culture.

On the morning of November 19 the patient suddenly collapsed. The heart was slightly dilated, with irregular rhythm due to the occurrence of dropped beats and extrasystoles. The temperature rose to 40.9 C. (105.6 F.). The pulse rate dropped to 70 beats per minute. In spite of supportive measures she died suddenly at 12 o'clock noon on November 19. An electrocardiogram taken two hours before death showed partial auriculoventricular heart block with dropped beats, bundle branch block on the left and ventricular premature beats.

After death numerous Klebs-Löffler bacilli were observed in the material from the throat in direct smear and on culture. Streptococcus haemolyticus was not noted. Cardiac blood on culture showed 6 colonies of C. diphtheriae per cubic centimeter in pure culture. Permission for postmortem examination was not obtained.

Bacteriologic Studies.—The organisms isolated from the throat and blood of the patient were compared with two other strains isolated from the throats of 2 patients with mild diphtheria, which also was contracted in Peiping during the fall of 1935. The observations in regard to morphologic structure, characteristics of the colonies, starch fermentation and hemolysis are briefly summarized in the following table. The cultures obtained from the throat and blood of the patient

Comparison of Strains of Organisms Cultured from Our Patient (1 and 2), the Patient's Brother (3) and Two Patients with Mild Diphtheria (4 and 5)

Culture Number	Morphologic Structure	Appearance of Colonies on Chocolate Tellurite Medium	Fermentation in Starch Serum Water*	Hemolysis on Horse Blood Agar Plates*
1 (Throat)	Short bacilli; polar bodies poorly stained	Grayish, flat, with slightly elevated center	+	—
2 (Blood)	Same	Same	+	—
3	Same	Same	+	—
4	Long bacilli; polar bodies well stained	Black, smooth	—	—
5	Same	Same	—	—

* In these columns + indicates that fermentation or hemolysis occurred, and — indicates that fermentation and hemolysis failed to occur.

are numbered, respectively, 1 and 2. The culture made from the throat of the patient's brother, who also died of diphtheria, is included as culture 3. Cultures 4 and 5 were isolated from the 2 patients with mild diphtheria.

Cultures 1 and 2, isolated from the patient, and the culture isolated from the patient's brother were identical. The reactions were characteristic of the gravis type of diphtheria bacilli, first described in England by Anderson and his co-workers in 1931.[5] The two strains, 4 and 5, isolated from patients with clinically mild conditions differed distinctly from cultures 1 and 2 in morphologic structure, characteristic of the colonies, ability to ferment starch and production of hemolysis; the organisms corresponded with the mitis type described by the English workers.

In addition to the foregoing methods of distinguishing between gravis and mitis types of diphtheria bacilli, certain authors have suggested that there is a difference in the degree of virulence of the two types for guinea-pigs and rabbits. Gravis strains were considered by Robinson and Marshall[6] to be more virulent than mitis strains for guinea-pigs on subcutaneous injection. Anderson and his associates[7] stated that gravis strains seemed more virulent than mitis strains for rabbits on intramuscular injection.

Cultures 1 and 2 and 4 and 5 were compared as to virulence. The growth on a Löffler slant of each of the four strains after eighteen hours was washed off in saline solution. The same dose, one eighth the amount of culture thus obtained, was injected into guinea-pigs and rabbits. Two guinea-pigs and two rabbits were inoculated with each culture. The guinea-pigs were given injections subcutaneously and the rabbits intramuscularly. All the animals died in a short time, and no striking difference in regard to the virulence of the two types of organisms was observed.

COMMENT

The case reported in this paper is, as far as we have been able to determine, the third in which septicemia or bacteremia due to pure diphtheria bacillus occurred during life. Like the 2 patients in the cases previously reported by Roedelius, this patient had purpuric manifestations. There was no direct connection between septicemia and purpura, however, since in the 12 cases reported by Roedelius in which the patient showed "hemorrhagic diathesis" and did not recover, blood cultures were sterile. The younger brother of the patient under discussion, who also died of faucial diphtheria due to organisms of the gravis type, had severe purpuric manifestations, yet blood cultures on two occasions were sterile. Recently Frank and Hartmann[8] studied the blood of

5. Anderson, J. S.; Happold, F. C.; McLeod, J. W., and Thomson, J. G.: On the Existence of Two Forms of Diphtheria Bacillus—B. Diphtheriae Gravis and B. Diphtheriae Mitis—and a New Medium for Their Differentiation and for the Bacteriological Diagnosis of Diphtheria, J. Path. & Bact. **34**:667-681, 1931.

6. Robinson, D. T., and Marshall, F. N.: Investigation on the Gravis, Mitis and Intermediate Types of C. Diphtheriae and Their Clinical Significance, J. Path. & Bact. **38**:73, 1934.

7. Anderson, J. S.; Cooper, K. E.; Happold, F. C., and McLeod, J. W.: Incidence and Correlation with Clinical Severity of Gravis, Mitis, and Intermediate Types of Diphtheria Bacillus in a Series of Five Hundred Cases at Leeds, J. Path. & Bact. **36**:169-182, 1933.

8. Frank, E., and Hartmann, E.: Maligne Diphtherie mit hämorrhagischer Diathese, Ztschr. f. klin. Med. **119**:460-476, 1932.

11 patients with malignant diphtheria associated with purpuric manifestations. The authors noted that the number of platelets was reduced and that the bleeding time was prolonged, with occasional absence of clot retraction. The hemorrhagic tendencies observed in cases of severe diphtheria can probably be attributed to toxemia and do not seem to differ from the purpura that may be associated with any severe infection.

The invasion of the blood stream by diphtheria bacilli in the case of Roedelius' 2 patients and in ours seemed to have been transitory, the condition being bacteremia rather than septicemia. In 1 of Roedelius' cases the patient recovered, and in the other a blood culture made post mortem was sterile. In our case the blood culture made post mortem showed a decided reduction in the number of colonies when compared with the culture taken during life.

The organisms isolated from the throat and blood of our patient were of the gravis type. In this instance our observations were in agreement with those of the English workers that the gravis type is often associated with severe diphtheria.

CONCLUSION

A fatal case of bacteremia due to C. diphtheriae of the gravis type is reported.

MENINGITIS DUE TO BRUCELLA IN A CHILD

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The presence of meningitis due to Brucella is rarely recognized in children. However, the disease probably is more common than the figures indicate; perhaps some of the conditions diagnosed as tuberculous meningitis in which no organisms were seen on direct smear or some of those diagnosed as influenzal meningitis in which the organisms were seen but not cultivated were meningitis due to Brucella. Of the twelve proved cases [1] reported, in only one did the patient recover, after an illness of from two to three weeks' duration; the patient later contracted transverse myelitis and at present is paralyzed below the midabdomen, with total paralysis of the extremities.[1h]

The patient whose case is described in this paper had low grade meningitis, and Brucella abortus (var. bovis) was isolated from the spinal

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1. (*a*) Hughes, M. L.: Mediterranean, Malta or Undulant Fever, London, Macmillan & Company, 1897, p. 125. (*b*) Lemaire, M. G.: Méningite à mélitocoques: Altérations importantes du liquide céphalo-rachidien, Bull. et mém. Soc. méd. d. hôp. de Paris **48**:1636, 1924. (*c*) Hartley, G. A.; Millice, G. S., and Jordan, P. H.: Undulant Fever Meningitis: Report of a Case with Recovery, J. A. M. A. **103**:251 (July 28) 1934. (*d*) Desage, Pellerin, and Vinerta: Un cas de méningite à mélitensis, Bull. et mém. Soc. méd. d. hôp. de Paris **50**:872, 1926. (*e*) Sanders, W. E.: Undulant Fever Meningitis: Organism in Spinal Fluid, J. Iowa M. Soc. **21**:510, 1931. (*f*) Hansmann, G. H., and Schenken, J. R.: Melitensis Meningo-Encephalitis: Mycotic Aneurysm Due to Brucella Melitensis Var. Porcine, Am. J. Path. **8**:435, 1932. (*g*) Noto, G. G.: Pachi-e leptomeningite cronica spinale adesiva consecutiva a meningite melitococcica, Riv. di pat. nerv. **40**:440, 1932. (*h*) Pons, C. A., in discussion on Hansmann, G., and Schenken, J.: Melitensis Meningo-Encephalitis, Am. J. Path. **8**:610, 1932. (*i*) Bingel, A., and Jacobsthal, E.: Ueber Meningitis bei Banginfektion ihr klinisches und bakteriologischserologisches Bild, Klin. Wchnschr. **12**:1093, 1933. (*j*) Moretti, A.: Sulle complicazioni nervose della melitococcia, Riforma med. **49**:1428, 1933. (*k*) De Jong, Russell N.: Central Nervous System Involvement in Undulant Fever, with the Report of a Case and a Survey of the Literature, J. Nerv. & Ment. Dis. **83**:430, 1936. (*l*) Poston, Mary A., and Smith, D. T.: Successful Treatment of Brucella Meningitis with Immune Human Serum: Isolation of the Organism by a Modified Cultural Method, New England J. Med. **215**:369, 1936.

fluid. She was treated with intraspinal injections of human immune serum [11] and has completely recovered.

REPORT OF A CASE

E. L., a white girl 7 years of age, was admitted to the Duke Hospital on Jan. 5, 1936, with the complaint of abdominal pain of six weeks' duration. The onset, on Nov. 20, 1935, was sudden, with sore throat, fever and vomiting. Three days later a violent frontal headache began, which caused her to cry out with pain. The neck became stiff and painful. After the removal of a small amount of clear spinal fluid by the attending physician, Dr. G. C. Bell, Wilson, N. C., the temperature fell to normal, and the headache and stiff neck disappeared. On December 18 the symptoms returned, and another lumbar puncture was done. It was learned after the patient recovered that gram-negative "influenza-like" bacilli were seen in smears of this spinal fluid, but that they could not be cultivated by ordinary bacteriologic methods. The spinal fluid was sterile on culture, and no organisms were seen in the direct smear. No improvement was noticed until December 25, when the stiffness of the neck disappeared, the appetite increased and the child was able to play about the house. The signs of meningitis reappeared on Jan. 4, 1936, and the patient was admitted to the Duke Hospital on the following day. On admission the child was well developed but somewhat undernourished and definitely ill. She lay in bed, with knees flexed, and resisted any attempt to be moved. The neck and back were stiff, and the tendon and abdominal reflexes were hyperactive. Brudzinski's sign was present; Kernig's sign was present on both sides, and there was inconstant ankle clonus on the left. Babinski's sign was absent, and there was no motor weakness. The hemoglobin content was 12.2 Gm. per hundred cubic centimeters (78 per cent Sahli). No parasites or other abnormalities were found in blood smears. The leukocyte count was 10,000, with 69 per cent polymorphonuclears, 21 per cent small lymphocytes, 3 per cent large lymphocytes, 4 per cent monocytes and 3 per cent eosinophils. The Wassermann test of the blood, the tuberculin test (0.1 mg.) and roentgen examination of the chest gave negative results. The urine contained a trace of acetone. No occult blood or parasites were found in the stool.

Lumbar puncture yielded cloudy fluid, containing 3,370 leukocytes per cubic millimeter, 61 per cent polymorphonuclears and 39 per cent mononuclears. The Pandy test was 2 plus, and the benzidine test was 1 plus. Smears and cultures of the spinal fluid made by ordinary methods were negative. Lumbar puncture performed on January 9 yielded fluid that on examination gave essentially the same results. However, a special culture of this fluid [11] for Brucella yielded a growth after twenty-four hours of incubation. The organisms were agglutinated in a dilution of 1:640 by rabbit serum made with a stock bovine strain of Brucella. On January 14 more spinal fluid was removed, and again a positive culture was obtained. At this time 13 cc. of fresh immune serum, which agglutinated the organism isolated from the spinal fluid in a dilution of 1:640, was introduced intraspinally. Fifteen hours after the first injection of serum, the temperature rose to 39.5 C. (103 F.); it then fell to normal and remained so. The treatment was repeated on January 15, 18 and 22, making a total dose of 61 cc. of serum. The spinal fluid observed on each of these occasions was slightly cloudy; no growth was obtained, and the total white cell count fell to 199, with a decrease in the percentage of polymorphonuclears. There was steady symptomatic improvement, and lumbar puncture on January 28 yielded clear fluid, with no increase in pressure, containing 157 white cells, all mononuclears.

Two blood cultures were negative, and the patient's serum did not agglutinate her own or stock organisms. A cutaneous test with killed Brucella organisms gave negative results. An autogenous vaccine was prepared, and after a series of injections the patient's serum agglutinated her own and a stock antigen in a dilution of 1 : 80. The patient was discharged on Feb. 5, 1936, free from symptoms.

SUMMARY

1. Brucella abortus (var. bovis) was proved to be the etiologic agent in a case of low grade subacute meningitis in a child.

2. Complete recovery was obtained after intraspinal injections of human immune serum.

3. The child then was actively immunized (as was indicated by positive agglutination) by inoculations with autogenous Brucella vaccine.

Progress in Pediatrics

EARLY DIAGNOSIS AND NONSURGICAL TREATMENT OF STRABISMUS

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In January 1932 the problem of determining the efficiency of the nonsurgical treatment of strabismus was presented to the Northwestern University Medical School by the Section on Ophthalmology of the American Medical Association and the American Academy of Ophthalmology and Otolaryngology. To study this problem an orthoptic clinic was begun at Northwestern University under the supervision of Dr. Sanford Gifford, and a second clinic was established at the Children's Memorial Hospital under the supervision of Dr. Richard Gamble. From these clinics five hundred and seven patients with concomitant squint have been treated by nonsurgical methods, and records of their progress or lack of progress recorded.

The data from these clinics are included in several papers by me.[1]

The purpose of this paper, however, is not to discuss the data but to emphasize: (1) the difference between the normal ocular deviations and strabismus, (2) the fact that concomitant squint usually appears gradually, (3) the fact that squint seldom recovers spontaneously and (4) the inadvisability of deferring the treatment of strabismus "until the child can cooperate."

NORMAL DEVIATIONS VERSUS STRABISMUS

Authorities believe that at birth the neuromuscular mechanism for coordinated ocular movements is poorly developed. Thus the temporary aimless movements of an infant's eyes often seen by all pediatricians probably produce diplopia. The tiny babe soon learns to see and fuse into a single image the two retinal images. Even after this ability to

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1. Guibor, G. P.: Some Possibilities of Orthoptic Training, Arch. Ophth. **11**:433-455 (March) 1934; Possibilities of Orthoptic Training: Further Report, Am. J. Ophth. **17**:834-839 (Sept.) 1934; Practical Details in the Orthoptic Treatment of Strabismus, Arch. Ophth. **12**:887-889 (Dec.) 1934; Strabismus in Children Corrected by Refraction Alone, Am. J. Ophth. **18**:944-949 (Oct.) 1935.

fuse exists there are temporary deviations of the eyes, which should cause no concern. These should be differentiated from a pathologic deviation, which is called strabismus, the cause of which should be investigated and removed. In the table a differential diagnosis between these two types of deviation has been made. The physiologic deviation appears during the first year and a half. It is temporary and usually bilateral and is seldom in a definite direction. It probably is due to an underdevelopment of the neuromuscular mechanism associated with sudden relaxation of the muscles of the eye for short periods. The final results of the physiologic ocular movements in the infant are normal vision, parallel eyes and good fusion of images.

Differential Diagnosis Between Physiologic Ocular Movements and Abnormal Deviations (Strabismus)

	Physiologic Deviations	Strabismus
Age at onset.....	First 18 mo. (potential squint)	After first year
Duration.....	Temporary (lasts only a few seconds)	Temporary and progresses gradually; becomes constant over long periods
Monocular or binocular.	Both eyes usually affected	Usually monocular (85 per cent of cases)
Direction of deviation...	Variable (never constant)	Constant; assumes a definite direction in, out, up or down
Distant or near vision...	?	At first for near vision, gradually for far vision
Predisposing causes.....	Undeveloped neuromuscular ocular mechanism for maintaining binocular vision (theoretical)	1. Heredity 2. Hypermetropia 3. Muscular defects 4. Asymmetrical retinal images 5. Fusion defects 6. Amblyopia
Exciting causes.....	Temporary incoordination due to relaxation of muscles (theoretical)	1. Close work (reading) 2. Infectious diseases
Results of deviations....	1. Normal vision 2. Parallel visual axis 3. Binocular vision	1. Permanent deviation 2. Frequent unilateral amblyopia 3. Contraction and hypertrophy of muscles associated with relaxation of opposing groups 4. Absence of binocular vision 5. Psychologic changes (inferiority complex)

But the onset of strabismus usually occurs after the first eighteen months. It may appear during the first year. In many cases it begins at the age of 2 years and is especially noticeable at 5 years, when the child becomes interested in near work, which requires accommodative effort, and when resistance is low from some infectious disease.

It occurs at first as a slight temporary convergence or divergence, then becomes more pronounced and finally is constant. It is usually present in one eye but may become alternating. It assumes a definite direction, such as toward the nose (convergent), away from the nose (divergent), upward (sursumvergent) or downward (deorsumvergent)

and sometimes occurs in a combination of these directions. It appears for near work and then gradually becomes constant for both far and near vision.

The predisposing causes of strabismus seem to be many, the more important of these being (*a*) far-sightedeness; (*b*) abnormal muscular variations; (*c*) anisometropia and differences in the size of the retinal images of the two eyes; (*d*) defective ability for fusion; (*e*) amblyopia, or poor vision, and (*f*) a hereditary tendency to squint. These predisposing causes may be present long before the squint appears. But strabismus may appear later when close work is attempted. Therefore, the mere fact that a squint is present is not the most significant fact which is emphasized in the table. The squint may be eliminated by operation. Several more important points, however, are shown. If squint exists for six months or more, useful vision may be lost (amblyopia) in the crossed eye, and definite neuromuscular inability to hold the eyes straight occurs. The squinter loses the ability to see with both eyes simultaneously (binocular vision). This loss of binocular stereoscopic vision is noticed when the child plays marbles or baseball. He is unable to shoot the marbles straight and is seldom able to catch the ball.

In addition to these physiologic defects are the psychologic defects, which become manifest as an inferiority complex. This complex is often produced by playmates who call the boy "cock-eyed" and who tease and ostracize him. Thus few cross-eyed persons become executives or hold responsible positions unless the objectionable defect is lessened or eliminated. Even if the squint is eliminated, few large corporations keep men in responsible positions when the poor vision in the amblyopic eye is discovered.

STAGES OF SQUINT

Donders noticed that most infants show physiologic ocular deviations. This period of the physiologic deviations he called the "potential strabismus period." As has already been suggested, in an extremely small percentage of cases does squint begin during this period of life. These physiologic deviations usually result in a normal ocular mechanism unless some of the previously mentioned predisposing causes are present. If they are present one eye assumes a definite position, usually nasal (convergent strabismus), for short periods.

Thus the second, or periodic, stage begins. So far there has been no diminution of vision (amblyopia) and no change in the length of the extra-ocular muscles. The periodic stage is therefore the ideal time in which to treat the strabismus, because the muscular spasm and temporary suppression of the eye can be easily overcome by nonsur-

gical means, and complete recovery from the squint will occur. This stage may persist from one month to several years.

If no treatment is given during this stage the stage of fixed habit occurs. The squinting eye gradually assumes the abnormal position for long periods and frequently until it is seldom parallel with its fellow. By this time the patient is perhaps 3 years of age. He seldom uses the squinting eye and is losing the vision in it. Even then the squint may not be constant and one hopes that the condition will improve. This hope, however, is often in vain. This stage of fixed habit may last one or two years.

If no treatment is given the degenerative stage occurs. The vision becomes dim; the external rectus muscle on the affected side becomes lengthened and the internal rectus muscle contracted. In this way, therefore, the squint which was an apparently innocuous temporary deviation of an eye becomes a serious deformity with partial loss of vision that is seldom relieved by glasses, loss of stereoscopic ability and, finally, definite elongation of muscles and contracture of their opponents. In this degenerative stage, therefore, if a squint is severe little can be accomplished by nonsurgical means. If the angle of squint is great and a visual defect or a severe muscular abnormality persists, one or more operations may be necessary to correct the deviation.

The mechanism which produces convergent strabismus in many cases should be understood (fig. 1). There is first an overaction of the internal rectus muscle caused by an overaction of accommodation, neither of which exists constantly at first before the stage of fixed habit appears. This relationship between accommodation (which is the power of the eyes to focus rays of light on the retina) and convergence (which is the power of the internal rectus muscles to rotate the eyes toward the median line) is well known. When an emmetropic person looks at a distant object there is no accommodation or convergence, as is shown in figure 1 *A*. When the emmetrope looks at a near object the lens within the eye becomes thicker in its anteroposterior diameter, and the anterior segments approach each other. If convergence did not occur, double vision for near objects would be present. At 13 inches (33 cm.) from the eye the emmetrope accommodates 3 diopters and converges 3 meter angles. This is a normal relationship.

On the other hand, a far-sighted eye will focus rays of light posterior to the retina if accommodation is relaxed (fig. 1 *B*). Therefore, in a far-sighted eye accommodation for viewing distant objects is necessary in order to focus them clearly on the retina. This increase of accommodation causes a reflex increase of convergence. At times this becomes so severe that the squinter looks at the object with one eye, while the other eye is suppressed and squints nasally owing to the overacting internal rectus muscles (fig. 1 *C*).

This is not the only mechanism producing strabismus but for my purpose will demonstrate how important it is to make an early accurate examination of the eyes under the influence of a cycloplegic to determine whether hypermetropia is present. If advisable, corrective lenses should be worn to overcome any hypermetropia and the resulting increase of accommodation and convergence from uncorrected farsightedness.

All these factors indicate that the treatment of strabismus should begin as soon as possible after the diagnosis is made. The familiar suggestion given to the parents that an infant will outgrow the squint is a mistake, because, as can be seen in the table, partial loss of vision and secondary muscular degeneration occur in many cases. There are

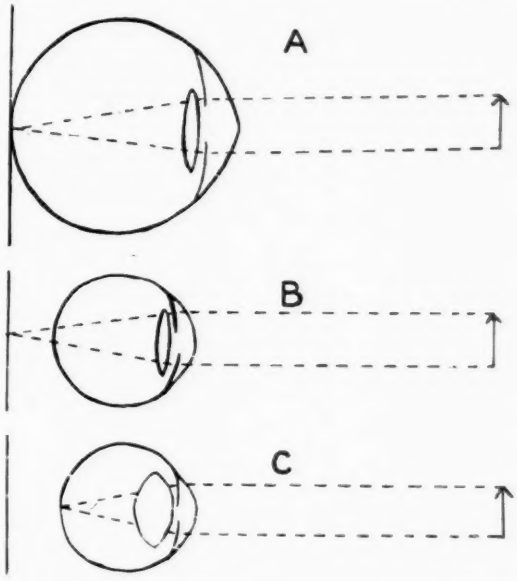

Fig. 1.—Diagram showing the increased accommodation necessary in order to focus distant objects on the retina in hypermetropic astigmatism. *A*, normal eye relaxed; distant objects focused at a point on the retina. *B*, hypermetropic eye relaxed; distant objects not focused at a point. Note the thickness of the lens. *C*, hypermetropic eye accommodating for far vision, in order to focus distant objects to a point on the retina. Compare the thickened lens with the lenses in *A* and *B*.

four nonsurgical methods for treating strabismus. These are atropinization of the eyes, occlusion of the fixing eye, correction of the refractive errors and orthoptic fusion exercises.

ATROPINIZATION AND OCCLUSION

The treatment of the extremely young infant or the uncooperative child is atropinization or occlusion of the fixing eye. A 0.5 per cent

solution of atropine sulfate or 1 per cent atropine ointment, if placed in the straight eye once a month, will overcome convergent strabismus in four or five months in some cases. When the mother notices that one eye is squinting she places the solution or ointment below the upper lid of the straight eye. If the child is uncooperative the medicine can be put in the straight eye while he is asleep.

CORRECTION OF AMETROPIA

The third step in the nonoperative treatment is the examination and correction of the refractive errors. Atropine is placed in both eyes three times a day for three days preceding the refraction. All ophthalmologists believe that a cycloplegic examination is essential for children in order to make possible an accurate diagnosis of the condition and a correction of the errors of refraction. Examination of the fundus too is necessary to determine whether there is a defect in the macula. If a defect in the retina is present, nonoperative treatment is contraindicated, and surgical treatment is indicated. Children as young as 1 year old are infrequently examined. These cases are exceptions. Yet it is well to attempt the examination if the child will sit still and not close the eyes. In such an examination the minimum of cooperation is required from the patient. The complete degree of ametropia can be determined, the correct lenses prescribed and the fundus examined.

If glasses are needed they should be prescribed and worn as early as 1 year of age. The vision of these infants is so improved by glasses that many of them will cry when the lenses are removed. In most instances, therefore, the parents will have no difficulty in making the patient wear the glasses. I have never seen a child's eye lost by a lens' being broken and entering the eye. At present there are nonshatterable lenses, which will lessen such dangers.

Of what benefit are these glasses in correcting the squint?

First, vision is improved in both eyes. In older children, in whom the improvement in visual acuity can be measured, the unaided vision of 20/50 may be improved to 20/20 at times by correct lenses.

Second, the excess accommodative effort in hypermetropia which causes the excess convergence may be eliminated completely by the lenses while the glasses are worn (fig. 1 *A*, *B* and *C*). In such cases the visual axes may become parallel and ability for fusion develops spontaneously. The possibility of elongation of the external rectus muscles and of contracture of the internal rectus muscles is thus lessened.

Glasses, atropinization and occlusion seldom correct squint in cases in which amblyopia occurs in the squinting eye, those in which severe

contracture of the internal rectus muscle exists or those in which a severe defect in the ability for fusion is present. In such cases glasses may be prescribed to improve the vision, but atropinization and occlusion of the fixing eye must be used to compel the patient to use the amblyopic eye. Similarly, atropine can be used in both eyes to relax the accommodation. If no improvement is noticed after months of atropinization, the fourth routine in the nonsurgical treatment, which is called fusion training, must be employed. The details of this training are so tiresome that I shall omit them.

FUSION TRAINING

This type of treatment is used for patients as young as 3 or 4 years of age if the child will point to the objects which he sees in the

Fig. 2.—Type of strabismus aided by glasses and orthoptic exercises. *A* shows 50 degrees of accommodative strabismus in the right eye without glasses. *B* shows 50 degrees of accommodative strabismus in the left eye without glasses. *C* shows the eyes with the accommodative factor removed with glasses; convergence is slight in the right eye. Squint recurs without the glasses.

instrument. For all ordinary cases the stereoscope is used with especially prepared diagnostic and therapeutic charts. Other instruments are often used.

The efficiency of these nonsurgical methods of treatment has been determined. If the routine of atropinization, correction of the refractive errors, occlusion and the use of fusion exercises is employed energetically, 50 per cent of the patients will recover without the aid of surgical intervention.

REPORT OF CASES

In conclusion I shall report three cases. In the first two the strabismus is of the type which is aided by nonsurgical means. In the last the strabismus is of the most difficult type, and the patient will recover only after several operations. For my purpose at this time the details of the refractive correction and the history

are unnecessary. The photographs in figure 2 show a patient with alternating convergent squint of 50 arc degrees. This squint is due mainly to uncorrected high hypermetropia associated with overacting internal rectus muscles. The mechanism producing this type of strabismus is demonstrated if one studies figure 1 *A*, *B* and *C*. The increased accommodative effort necessary to focus objects clearly on the retina of the far-sighted person produces increased convergence. In figure 2 *C* the glasses reduce the increased accommodative effort, and the squint becomes negligible. The advantages of the glasses in a case like this so far outweighs their disadvantages that the lenses should be prescribed as early

Fig. 3.—Type of strabismus aided by glasses, atropine and fusion exercises. *A* shows convergence of 40 degrees with sursumvergence of 15 degrees in the left eye without glasses. *B* shows the appearance after recovery two years later.

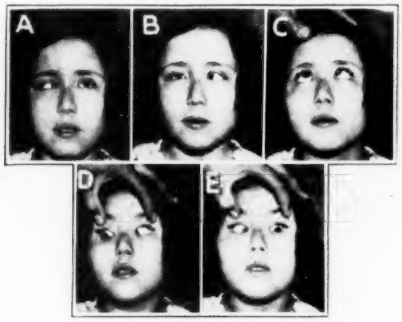

Fig. 4.—Type of strabismus unaided by nonsurgical treatment. The strabismus is alternating. Note the multiple muscular abnormalities. *A* shows convergence of 50 degrees in the right eye, due to overaction of the right internal rectus muscle. *B* shows convergence of 50 degrees in the left eye, due to overaction of the left internal rectus muscle. *C* shows appearance due to overaction of the left inferior oblique muscle. *D* shows the appearance due to overaction of the left superior oblique muscle and underaction of the right inferior rectus muscle and the right external rectus muscle. *E* shows appearance due to overaction of the right superior oblique muscle and underaction of the left inferior rectus muscle and the left external rectus muscle.

as the eyes can be tested under the influence of a cycloplegic. Thus, even for an infant 1 year of age, if the degree of far-sightedness can be determined the glasses should be prescribed and worn.

Figure 3 *A* shows a boy with a left convergence of 40 arc degrees and slight sursumvergence of 15 arc degrees. After he wore his glasses the strabismus was much improved, but squint of 40 arc degrees still existed. After atropinization and occlusion of his right eye for two years the visual axes became parallel.

The five photographs in figure 4 show a patient with alternating strabismus of 50 arc degrees. The internal rectus muscles, the inferior oblique muscles and the superior oblique muscles are all overactive or hypertensive. Both the external rectus muscles are markedly underactive. In such a patient the squint is not improved by nonsurgical means. Surgical measures will lessen the severity of the strabismus, but a number of operations will be necessary to accomplish marked improvement.

SUMMARY

A comparison between the physiologic and pathologic ocular deviations is made. The physiologic deviations are not constant in time of appearance, in direction and in duration and disappear spontaneously, while strabismus shows a constancy of deviation and direction, is progressive and rarely appears suddenly. Most patients do not recover spontaneously.

The anatomic defect called strabismus is serious. The more important associated defects are: unilateral amblyopia, loss of binocular vision, changes in the extra-ocular muscles and an inferiority complex.

The early diagnosis and treatment of the strabismus prevent or lessen the severity of these defects.

The nonsurgical orthoptic treatment of squint consists of atropinization, occlusion, correction of the refractive errors and fusion exercises.

In about 30 per cent of the cases strabismus can be corrected by refraction, atropinization and occlusion.

In about 50 per cent of the cases it can be corrected by those means plus orthoptic exercises. This figure is greater for squint below 15 degrees (83.4 per cent) and much lower for squint over 15 degrees (16 per cent).

Dr. Sanford Gifford and Dr. Richard C. Gamble gave assistance and aided by supervision during the last eighteen months in the clinics at the Children's Memorial Hospital and at Northwestern University, and Dr. Joseph Brenneman made many suggestions.

SPECIAL ARTICLE

DEDICATION OF THE ABRAHAM JACOBI-CARL SCHURZ MEMORIAL PARK

Bolton Landing, on Lake George, June 13, 1936

DEDICATION EXERCISES

Introduction

Dr. Henry L. K. Shaw, Albany, N. Y.
American Pediatric Society

Presiding

Dr. Frederic W. Schlutz, Chicago, Ill.

Chairman Abraham Jacobi Memorial Committee
Section on Pediatrics, American Medical Assn.

Addresses by

Dr. Isaac A. Abt, Chicago, Ill.
American Pediatric Society

Dr. Frederic E. Sondern, New York, N. Y.
Late President, Medical Society of the State of New York

Dr. Dixon Ryan Fox, Schenectady, N. Y.
President, Union University

Honorable George McAneny, New York, N. Y.
Carl Schurz Memorial Foundation

Transfer of the Memorial Park
By
Mrs. George McAneny (Daughter of Dr. Jacobi)
To
Hon. Edward M. Vandenburg
President, Village Board, Bolton Landing

Reception and Tea at the Residence of
Mr. and Mrs. George McAneny

OFFICIALLY DESIGNATED REPRESENTATIVES

American Pediatric Society	
Dr. Henry L. K. Shaw	Albany
Dr. Isaac A. Abt	Chicago
American Medical Association	
Dr. William J. Mayo	Rochester, Minn.
Dr. Arthur Dean Bevan	Chicago
Dr. Alexander Lambert	New York
Dr. Arthur W. Booth	Elmira, N. Y.
Medical Society of the State of New York	
Dr. Charles Gordon Heyd	New York
Dr. Charles Stover	Amsterdam
Dr. Martin B. Tinker	Ithaca
Dr. Thomas H. Halsted	Syracuse
Dr. Grant C. Madill	Ogdensburg
Dr. J. Richard Kevin	Brooklyn
New York Academy of Medicine	
Dr. Herbert Willy Meyer	New York
Dr. Philip Van Ingen	New York
Glens Falls Academy of Medicine	
Dr. Thomas H. Cunningham	Glens Falls
Dr. Morris Maslon	Glens Falls
German Medical Association	
Dr. Paul Kurt Sauer	New York
Dr. Armin V. St. George	New York
Carl Schurz Memorial Foundation	
Ferdinand Thun	Reading, Pa.
Wilbur K. Thomas	Philadelphia
George McAneny	New York

The dedication exercises of the Abraham Jacobi-Carl Schurz Memorial Park were held on June 13, 1936, at Bolton Landing, on Lake George, N. Y. Dr. Henry L. K. Shaw, of Albany, N. Y., called the meeting to order.

DR. SHAW: The American Pediatric Society came to Lake George thirty-one years ago. Its host was Dr. Abraham Jacobi, who greeted us in person on that occasion. Today the American Pediatric Society again visits Lake George to hold its annual meeting. Abraham Jacobi is with us not in person but in spirit.

Twenty-nine members of a total of fifty-eight were in attendance at the 1905 meeting. Of an active membership of ninety-five, sixty-nine members and eleven emeritus members are in attendance at this 1936 meeting. We have also with us, for the first time, the members of the Canadian Pediatric Society. We have enjoyed the presence of our Canadian cousins on this occasion, and I think it safe to say that over one hundred and fifty specialists in diseases of children, from all parts of the United States and Canada, have gathered here not alone for scientific discussion but also to do homage to the memory of our beloved Abraham Jacobi.

A few words as to the origin of this memorial. Three years ago, when I was in this vicinity, I made a pilgrimage to the home of Dr. Jacobi and at the entrance found a beautiful marble bench in memory of Carl Schurz. He was a life-long friend and companion of Dr. Jacobi and lived in an adjoining house. They both loved this place and together wandered through these woods. It seemed to me that the physicians of this country were more than remiss in not erecting a permanent testimonial of their love for Abraham Jacobi. The Section of Pediatrics of the American Medical Association had founded the Abraham Jacobi Memorial

Fund shortly after his death. The object of this fund was to bring pediatrists of international reputation to lecture before the society. I wrote to Dr. Frank Neff, the treasurer of the fund, and explained the situation. He became interested at once and made a trip to Bolton Landing to look over the situation. He agreed with me that a memorial should be erected to Abraham Jacobi. His interest and counsel were an inspiring help.

The administrators of the Jacobi memorial fund agreed to pay the expenses of this undertaking. The question then was to decide what form the memorial should take. The first idea was to provide a bench similar to the Carl Schurz bench, to be placed at the other side of the entrance to the Jacobi-Schurz estate. This

Fig. 1.—Abraham Jacobi.

proved not to be feasible, and Mrs. McAneny proposed the present site. This is one of the spots they loved, and they had named it the Schwarzwald. Mrs. McAneny said she would be glad to dedicate this property for the site of a memorial to Abraham Jacobi and Carl Schurz provided it could be preserved and looked after in the future. The village board of Bolton Landing held a meeting and agreed to include it as part of their park system; so this memorial park will grow more beautiful each year and will be cared for by the trustees of Bolton Landing.

I wrote to several of Dr. Jacobi's friends about this plan, and I wish I had time to read some of the replies. I have never done anything that received so

cordial a reception as did the plan of this memorial to Abraham Jacobi. A number of these friends are here today, as well as officially designated representatives of medical organizations in which Dr. Jacobi had served as president and had been an active and valuable member. A few such representatives were unable to be present and sent their regrets. In this connection, I should like to read part of a letter received from Dr. William J. Mayo, of Rochester, Minn. He wrote: "I am so pleased that this tribute is to be paid to Dr. Jacobi, one of the pioneers in pediatrics. He was a sound medical man and educator and a valiant fighter for educational methods."

Many distinguished visitors are here to do homage to the memory of Abraham Jacobi. Dr. Charles Gordon Heyd, of New York, president of the American Medical Association; Dr. Edward Godfrey, commissioner of health of the state of New York; Dr. Grant Madill, regent of New York University, and many others have journeyed here to attend this dedication.

The Carl Schurz Memorial Foundation of Philadelphia is represented by its secretary, Dr. Wilbur K. Thomas. This association made possible the removal of the Carl Schurz bench to the new location; so the memories of two old patriots who in life were so closely united by the bonds of friendship are now joined after death.

I should be entirely failing in appreciation if I did not mention our landscape gardener, Mr. Robert Cassidy, who for the past six weeks has worked untiringly and has transformed this spot. He has kept the spirit of the woods in his arrangement of the shrubs, ferns and wild flowers.

What little I have done has been a labor of love, and it has been one of the great joys of my life. "I have gathered a bunch of other men's roses, and only the cord that binds them is my own."

I take great pleasure in introducing Dr. Frederic W. Schlutz, professor of pediatrics at the University of Chicago and chairman of the Abraham Jacobi Memorial Fund, who will act as chairman of this meeting.

Dr. Schlutz: We are meeting here today to honor the memory of two men whose achievements, measured by any standard, are remarkable. Coming to this country as exiles, seeking freedom of thought and action, both found it and became eminent figures in our national life. The one was distinguished as a soldier, statesman and writer, the other as a beloved physician and leader in his profession.

Carl Schurz belongs to American history. Probably only a few here today knew him as a man and companion. Abraham Jacobi belongs to us. The majority of those present knew him and are gathered here to honor the memory of the beloved founder, leader, teacher and friend. Who can forget the small, frail figure with the massive head and wind-blown hair, and the eagle glance of his eye betokening indomitable spirit and the courageous heart?

The lasting friendship of these two men for each other, terminated only by death, is one of the lovely tributes and inspirations of their noble characters. Companions from their earliest days, they shared joy and sorrow alike and exhibited that communion of spirit which is the outstanding mark of true friendship.

There is a tender significance in connection with our meeting in this place. In this lovely vale, among these whispering pines, along the shores and the placid waters of this beautiful lake, in the shadow of the surrounding verdant hills, these two fine souls communed, lived and dreamed.

Here they came to rest from their labors and the turbulent strife and turmoil of the day. We can sense the presence of their spirit on this occasion. Every foot of this ground is sacred to their memory. It is eminently fitting that we gather here today to dedicate this lovely spot and these memorials in granite and bronze to their perpetual memory.

The committee carefully searched for those who could befittingly speak on this memorable occasion. Dr. Jacobi was dear to us, as medical men, and was revered as a great leader, teacher and physician and a most honorable exponent of the ancient art of medicine.

I call on one of his oldest friends, one who in a measure has succeeded him, Dr. Isaac Abt, of Chicago.

DR. ABT: We are met today to dedicate a memorial to Abraham Jacobi, to pay tribute to that great pathfinder, humanitarian, writer, teacher and physician. It is especially fitting on this occasion that pediatrists gratefully express their appre-

Fig. 2.—The marble bench in memory of Carl Schurz and the stone bearing an inscription to Abraham Jacobi. The two friends called this site the Schwarzwald.

1830 **In Memory of** 1919

ABRAHAM JACOBI

Occupied the First Chair of Pediatrics in America
A Scholarly and Broad-minded Physician
Once President American Medical Association
Erected by his Friends and Colleagues
The Abraham Jacobi Memorial Fund
The American Pediatric Society
June 13, 1936

1829 **To the Happy Memory of** 1906

CARL SCHURZ

Soldier - Statesman - Scholar - Patriot
For fourteen summers, 1892-1905, he achieved
and rested in these precincts whose beauty
was his never ending joy.
Erected September, 1925

ciation of his leadership, for it was Abraham Jacobi who laid the foundation of pediatrics on this continent, and no one has exercised a wider or more permanent influence in that field than he.

It is not only America, his adopted land, that owes him a debt of gratitude. His influence was international. He contributed to the medical literature of Germany. An accomplished linguist, he addressed the international congress in France in the language of that country. Some of his writings have been translated into Italian and Russian.

His collected works, eight volumes of essays and addresses, have found a notable place in medical literature. It has been said of much of Jacobi's work, especially of that pertaining to the feeding of infants, that it was advanced in character.

Fig. 3.—The inscription in memory of Abraham Jacobi.

Perhaps the clue to his virile and original mental constitution may be found in the political and social background of the Europe into which he was born in the year 1830. In his youth he witnessed the famine of 1845-1846, the ensuing financial depression and political discord and the revolutions and storms that swept nearly all of central Europe during 1848 and 1849.

It will be recalled that although after the defeat of Napoleon the Congress of Vienna had recommended the granting of a constitution in Austria and in Germany, owing to the subversive influence of Metternich, Chancellor of Austria, these rights were withheld and freedom of speech and of the press and personal liberty of every kind were suppressed.

The Carlsbad Decrees of 1819 had practically put an end to academic freedom. All university publications were subject to censorship, and the professors were secretly watched to make sure they taught nothing of which the government did not approve.

The fires of discontent smoldered until 1848. An outbreak in Paris was followed by revolution in Vienna and Berlin. Frederick William IV of Prussia was forced to grant a constitution, and in Vienna Metternich was deposed.

For years the United States had been the center of liberal learning and utterances. In Germany professors and students suspected of radical tendencies were relentlessly persecuted. Thousands of leading spirits, men who had already made names for themselves in science and letters, were compelled to flee to other countries. Two years after his graduation Abraham Jacobi was held in detention in Germany, during the restlessness at Cologne and Minden, for revolutionary activities.

Escaping first to England, he eventually reached these hospitable shores, where many of Germany's distinguished citizens—her most intelligent and highly educated men, professors, students, educators, ministers and artists, all men of high ideals—had already found refuge. Through his long career Abraham Jacobi consistently manifested the characteristics which distinguished his youth; love of liberty, abhorrence of oppression, belief in the struggle for human rights and the conviction that all people should be insured protection by law of their inherent privileges and freedom. Above all, he showed a passionate zeal for righteousness.

In the year 1853, when Jacobi landed in this country, he immediately found that education, as might be expected in a young land, was undeveloped. Specialization was little practiced. Most men were general practitioners. Teachers of medicine in the large centers taught surgery, medicine, diseases of women, diseases of the eye and the fundamental studies of physiology and anatomy. Instruction in diseases of children was hardly attempted. Such mixed instruction as was given was assigned either to the department which taught diseases of women or to the department of internal medicine.

Physicians went into practice with little knowledge of the nature and extremity of childhood diseases. This situation was viewed with complacency by the doctor as well as by the general public, although the sickness rates and death rates were appallingly high. The treatment of diphtheria, scarlet fever and dysentery was unavailing, owing to the empirical methods employed and the lack of knowledge as to the nature and cure.

Before the close of his career, and largely because of his own efforts, Jacobi had the satisfaction of seeing pediatric instruction carried on as a separate branch in almost every medical school in the country. He saw the awakening of a lively interest in the prevention and treatment of diseases of children. He saw scientific and clinical investigation in nutrition, growth and development and metabolism occupy an important place in medicine.

And, what was all important to him, he lived to see the practical results of the work he had initiated in the reduction of sickness and the death rate. However, these great results were not obtained without much sacrifice and valiant struggle. When his fine, discerning judgment told him he was right he invariably acted with the courage of his conviction, fearless and undaunted by whatever authority might be arrayed against him.

Witness his struggle with the lady managers of the Children's Hospital in New York City. He had noted the high mortality in infants' hospitals and had the audacity to announce his conclusion that a large institution is no place for a young

infant. He proved that the sickness and the death rate for infants were lower in poor tenement quarters than in large infant asylums. Although a member of the staff, he denounced the efficiency of the hospital, telling the lady managers during the heat of the controversy that he was not in the habit of being frightened by ill will, malice and wanton persecution. The price he paid for his courage was the loss of his position, but he was by no means defeated. In his report to the Medical Society of the State of New York in 1872 he called attention to the fact that infant mortality was three times higher in public institutions than for the general population. He advised giving up the large institutions and dispersing the abandoned infants or farming them out in private families.

The soundness of his reasoning and conclusions has been fully substantiated by subsequent developments. Nor were they solely directed along medical lines. In this respect he was like Osler, whom he admired and of whom he said: "To him medicine is not private or narrow business; he is the statesman in medicine, which is to him not a trade but a vocation and a religion of itself." Of himself he said: "I feel very serious about the questions concerning the elevation of my beloved profession and the safety of the commonwealth. Both are identical."

He brought his authority as president of the Medical Society of the State of New York to bear on such problems as child labor, occupational diseases and municipal sanitation and housing. He struggled for more and better public schools and urged the necessity of isolating patients with infectious disease. He was unalterably opposed to capital punishment and warned society to make no mistake unless it was in the direction of leniency and humanity.

Of medical mistakes he was wont to speak in a more ironic vein. Said he: "The young doctors may learn at the expense of their patients or may make the same mistakes one hundred times. One hundred mistakes are then called experience." Again, in condemning surgeons who performed craniectomy in the treatment of idiotic children, he said: "No lotion of soap and water will clean those hands; no power of corrosive sublimate will disinfect their souls." He once remarked: "Plato said, 'The most interesting book that could be written would be a treatise on the errors of mankind.' Let us see to it that our mistakes may not swell that book."

He was also critical of himself and could direct the thrusts of his keen wit toward himself when occasion arose. He wrote: "Babies are the most philosophic people. They live or die, crow or wail, without regard to the half-mile or more of books and pamphlets which have been written about them in all the centuries, in all countries in the course of a century."

His subtle and often quaint humor increased with the passing years, as did industry, his devotion to his beloved profession and his enthusiasm. I recall with delight my meeting Dr. Jacobi at the Detroit session of the American Medical Association in 1916. After he had visited the roentgenologic exhibit he expressed his eagerness to have me revisit it, saying, "I cannot tell you how grateful I am that I have been permitted to live long enough to see this miracle of X-ray come to pass."

I like to recall his closing remarks to the McGill students at Montreal: "Gentlemen, I have kept you long, but I like to talk to the young. If, however, you are of the opinion of Cicero, who said old age makes loquacity, please remember that I had to wait seventy-five years before I had this opportunity."

Withal, it should be remembered that Jacobi was a wise physician, a keen diagnostician. His opinion was eagerly sought in consultation. He was an outstanding teacher, attracting students from every part of the country, and an inspiration to young men, in whom he stimulated interest for the study of the diseases of infancy and childhood.

I like best to recall the remarks he made at the memorial for his dear friend Krakovitzer, for no word can better or more fittingly express the affection, respect and reverence which Abraham Jacobi himself inspired in all who had the good fortune to know him or to come within the sphere of his influence. So let these words, his own words, be spoken in his memory.

"Stand by the tomb of Krakovitzer. No fear ever shook him, no bribe ever tempted him. He was uncorruptible, even by friendship or love or desire. The applause of the masses never impressed him. He was great enough to have enemies, but he enjoyed the respect of friend and enemy alike. His character was unimpeachable, his universality acknowledged, his moral life in its broadest sense unexcelled. Humanity was his leading star. He was a great physician, but his principal greatness he achieved as a man in whom many powers were happily blended in mild harmony. Much had been given to him; much was demanded of him, and he gave it all. He will have a monument. That monument will be the sacred memory of his noble deeds."

DR. SCHLUTZ: Time, the great reaper, has dealt kindly with us on this occasion in that it has left us the man who was intimately associated with Dr. Jacobi in his early days as a practitioner and who probably knew him better than any one else as the great physician. The beneficent influence of the character of Jacobi on his colleagues is reflected in the high honors which our body has abundantly accorded him. I call on Dr. Frederic E. Sondern, of New York, formerly president of the Medical Society of the State of New York.

DR. SONDERN: Any memorial to my departed chief, Abraham Jacobi, recalls to my mind an occasion at the height of his brilliant career. May 5, 1900, now a few days over thirty-six years ago, the occasion of his birthday at three score years and ten, had been selected for a complimentary dinner to him, as "a fit occasion for a hearty manifestation of the esteem in which he was held and for the recognition of the services he rendered in various relations, as physician, educator and civic worker." Then, as now, Dr. Jacobi's friends gathered to pay homage to a truly human master mind.

It is an honor and a pleasure to voice gratitude for having known this erudite man and having been accepted as a friend. Of the original arrangements committee of seven, Gerster, Bryant, Crandall, Huber, Meyer and Scharlau, I am the only surviving member. Just as we stand now that small nucleus stood on the former occasion, surrounded by the larger general committee of sixty-nine, with a company of over four hundred friends, colleagues and eminent men to attest his achievement.

Joe Bryant was toastmaster, that genial powerful man who was Jacobi's strongest ally in the interest of organized medicine in general and of the New York Academy of Medicine and the Medical Society of the State of New York in particular. He directed attention to Jacobi's patriotic zeal in liberty's cause in fostering the birth of individual freedom. Can you visualize Jacobi's indignation in these days of increasing collectivism and bureaucratic control? How he would, if here, throw back that grand head of his and stand in modest eloquence for individual initiative, individual freedom and the restoration of a competitive economy under a free, decentralized and limited government.

William H. Thomson spoke of Jacobi as the physician, and Sir William Osler spoke of him as the scientist. It was evident throughout his career that his superb mind was well trained in the basic sciences, but what he excelled in was, with that cultural background, the art of medicine. As Osler said, he constantly gave the impression of honesty of purpose and sincerity in the faithful administration of an intellectual trust, and his professional spirit was always reflected on the nobler side. His record is so well known and so well recognized that, after the eulogy of Abt, no more can be said by me of his professional attainment.

President Seth Low of Columbia spoke of Jacobi in relation to medical education. He compared his dynamic force in the interest of bedside teaching with the energy of Commodore Vanderbilt, who, in possession of the Harlem and Hudson River roads, claimed that with superior railroad service he would dry up the Erie Canal and drive every boat off the Hudson River.

It was Carl Schurz who spoke of Jacobi as a citizen, his speech being a eulogy, indeed, of rare tenor. To quote but one sentence: "There has hardly been an earnest effort for the enforcement of correct principles of government or for the vindication of justice and right or against evil practices or demoralizing tendencies in our public concerns, since Dr. Jacobi became a citizen of this republic, that he did not vigorously support, no matter whether other people liked it or not or what it might cost him." Schurz was Jacobi's mentor in politics for all of half a century, but this did not mean submission necessarily to another's views, and many were the heated arguments prior to agreement. However, since the ideals of both were constantly in the interest of right, justice, honor, liberty and popular government, they were unfortunately too often on the losing side politically.

While Seth Low called attention to Jacobi's tender and true friendships, it was Schurz who sounded the clarion note of that sentiment which is, after all, the most pleasing part of this retrospect, particularly for those of us for whom the shadows are lengthening. It is in this very spot on the lake that he liked to commune with himself and also to give expression to his thoughts, in surroundings to which he was so tenderly attached. Every tree and every view had a memory. The crags far and near represented determinations, immediate or remote, distinct and fearless against the clear blue sky, not necessarily of optimism, but of faith in mankind. The rolling hills, some verdant and others barren, characterized life in general, with its varying degrees of accomplishment and trial. The long dark valleys were emblems of sorrow, of which he had his full share and which he bore with fortitude. Each bush and flower had its significance in the life of this stern, brilliant and forceful, but kindly, man.

His memory will ever be, at least to those who knew him, a lasting example, inspiration and comfort.

The world is the better for his having lived in it.

Dr. Schlutz: It is the gift of few to phrase adequately and put into words that will touch the human heart the great and noble deeds of man. On some, Providence bestows this gift to no ordinary degree. The committee has called on one of these, a man who can speak as a friend of both men whom we honor today, a man whose renown as a historian, educator and writer is known to you all and whose eloquence, I am sure, will move your hearts. I take pleasure in presenting to you Dr. Dixon Ryan Fox, of Schenectady, N. Y., chancellor of Union University.

Dr. Fox: I stand here in some self-consicousness, not only because of the overgracious words of the presiding officer but because an introduction with the title of doctor in such company makes a layman feel a sense of quackery.

It is true, as the chairman has said, that I speak as a friend of Dr. Jacobi and of Carl Schurz. I am one of that great body of continuing friends that will reach on and on throughout posterity; I represent those who admire them, those who respect the two great figures, but who were born too late to know them in the immediate charm and inspiration of their persons.

One stands today almost at the conclusion of the first century of the era of the child. One hundred years ago Friedrich Froebel was just finishing his plans for the first kindergarten in the world. The benevolent Earl of Shaftsbury was

entering on his many-sided mission on behalf of the unfortunate children of old England, the little millhands, the little workers in the mines, chained to their ore carts in black subterranean galleries, the chimney sweeps and the ragamuffins. Horace Mann and Henry Barnard were just about to begin their magnificent service that was to revolutionize American education in the common schools. Mann was to become the superintendent of schools in Massachusetts in 1837, and Barnard was to occupy a similar office in Connecticut beginning in 1838. But while these pioneers were toiling, in far away Westphalia a little boy was toiling too, in preparation of himself and his life, preparing to write his name with theirs on the roll of fame and honor.

In that generation the child was regarded as a little adult. He was expected at the dawn of consciousness to put his thought on life, death and the great hereafter. I am reminded of a passage from a primer in general use. The child was expected to scan and repeat this verse:

> Our days begin with troubles here; our life is but a span.
> Cruel death is always near, so frail a thing is man.

That was supposed to be the ideal outlook of the little child. Play was a human frailty, tolerated in some quarters but not in many. The bishops of the Methodist Church who founded their college in the state of Maryland near the end of the eighteenth century spoke unmistakably upon this point: "Let the student be indulged in nothing that the world calls play, for those who play when they are young will play when they are old." This was the attitude toward the free life, that a child was not supposed to live.

Just as those pioneers whom I have mentioned discovered that the child had a mind but that it was not an adult mind, just as they discovered that the child had rights, so it was the destiny of Dr. Abraham Jacobi to reveal, at least as far as this country was concerned, that the child had a body which was not the same as an adult body. I would not here imply that he was unconcerned as to human rights. The distinguished and eloquent speakers here this afternoon have unfolded portions of his great career and have spoken of his noble sentiment and contribution to great causes. He was ready, actively willing, to champion unpopular causes, but it was his peculiar distinction to be the first professor of the diseases of children in the United States and to open the first free clinic for children in this country.

I suppose if any contemporary of Froebel, the Earl of Shaftsbury, Horace Mann and Henry Barnard were to come back today he would be less surprised by the network of concrete roads that webs this county and state and the incredibly fleet machines that dart across it and less surprised by the magic force of electricity which communicates my voice to your ears now or by the radio or other devices of travel and communication than by the remarkable progress that has been made in cutting down the blight of infant death.

All who have traveled through old churchyards remember how the hopes of man—and woman—were blasted by disappointment year after year after year. It was a great thing for a man standing in the stream of human misery in the great country of his adoption to be able to stem that tide of infant mortality. No wonder that his admirers, those who by the competence of their professional learning know his contribution, have been eager and active in rearing here a time-defying monument.

Places have power so long as and so far as they move the emotions of mankind. This place, this well remembered Schwartzwald, has such power; these stately trees, this woodland beauty, make their contribution to the charm of this hill-girt

lake, well known to us but not too well known throughout the world. Had a Wordsworth walked its shores, peered into the starlike flowers along its winding margins, surveyed its flashing waters and its forest walls, this lake would be as well known throughout the world as are the lakes of Cumberland across the sea. This grove has its part in the beauty of a lake all too insufficiently celebrated in song and story. But its chief charm and its chief power are not in the loveliness of nature. They come from its human associations.

We have been told this afternoon by old friends how he whom we celebrate walked here; and he walks here still in memory, in influence and in inspiration. There has been reared a suitable and seemly monument, but there is to be here a monument more suitable and lasting than bronze and stone; for under this canopy and across this leafy carpet year after year and, it is hoped, century after century, little children will romp their way in gladness, and by the symbolism of their health and happiness they will be the permanent monuments of a man who gave a great career to save the lives of little children.

I am not unmindful that we celebrate today not only the contribution of one great career but the example and the inspiration of a notable and sacred friendship. These two men, Jacobi and Schurz, found companionship of mind beneath these trees, gave energy to their dreams in lofty plans, and these echoing hillsides are forever associated with the memory of two friends. They were liberals. Both had escaped from the fortress prisons of old and aristocratic Germany. They believed in liberty, and they came here knowing that America was an idea much more than it was a place. They were not interested in security, because they believed that if talent and character had their decent chance at opportunity they would win their own security, and they were disposed, predisposed and determined to guarantee that chance at opportunity.

They were, I suppose, to be called reformers. That is a word charged with some disrespect in history and in contemporary thought; nevertheless they were men who were willing to sacrifice their own comfort, their own peace, that they might be of service in making a better world. That willingness came, as one of the speakers has observed, not from optimism but from faith. They had the faith that whatever is could be better, and it was in that faith they lived their lives and expressed their power through the lives of others.

So we are today in the presence of a great idea as well as of the memory of two distinguished personalities. Those who have gathered here from every corner of the country, those who have come to pay their tribute of respect, do so in large part because there walked here, and eternally shall walk in the memory of men so long as men shall read, two men who had the faith that by the effort of the human mind and by the impulse of the human heart things that are can, all of them, be better. With that blessing of hope exerted by these spirit voices through the air this afternoon, we feel the charm and power of this place.

It is a delusion to say there is absolute death. It was a favorite thesis of the stoics that strong personalities survived that great adventure and lived according to the power they had generated. It is certain that more potent here today than any living mind gathered in this tribute is the continuing influence that laughs at death, that carries on and on and on through the impulse it has made. In the mind of a philosopher there may not be much reality in this company of one hundred friends, but there is a deep reality in the influence of those strong spirits who are beckoning us, indeed driving us, with the power of their zeal and faith to make things that are better than they have been.

DR. SCHLUTZ: It is a peculiar pleasure and gratification if, on a memorable occasion like this, a member of the immediate family can be present to witness the

kind deed when man wishes to honor his fellowman. The son-in-law of Dr. Jacobi is with us today. He has contributed to and has nobly exemplified and carried on the traditions which so greatly distinguished the name of Jacobi.

Rising to the highest eminence in his own profession, he has been honored by many positions of trust in his own state and is noted for his benefaction and his interest in the public welfare. I have the great honor and pleasure of introducing to you The Honorable George McAneny, of New York, the son-in-law of Dr. Jacobi.

Honorable George McAneny: If I were to attempt to add to the glowing and moving words that have been spoken here today—to add to them in kind—I feel that I should fail sadly. But between them, so to speak, and representing that happy and fortunate group of the doctor's family and friends who here knew him so well, I may perhaps find some things either to emphasize or to repeat in other language that will bring to you some nearer reminder of those happy days.

I am asked to note my appearance, formally, as representing the Carl Schurz Memorial Committee, of which for a long time I served as chairman, as well as the present day Carl Schurz Memorial Foundation, which has very gladly contributed to the funds you have raised for your purpose of today and of which the director, Mr. Wilbur Thomas, of Philadelphia, is also here.

Returning again to the two great men you have come to honor, it might prove difficult indeed not to emphasize in some degree the significance of their lives and their places in history before I come back to these woods that they loved and to this scene.

It was a remarkable story of coincidence and of what one calls "teamwork," spiritually and otherwise, the work of these two. Both were born in the Rhineland, but a year apart; both fought nobly for the cause of liberalism during the troubled years of 1848 and those that followed; both found their refuge and their life-long home in America. Schurz, certainly since the Civil War, was among the first, if he was not the first, in standing of those who in public life contributed toward the mending of political and civil ills. Jacobi was certainly among the first of those who contributed toward the lessening and the alleviation of bodily ills and of the ills of society.

Indeed, these two names shine alike against the great background of the history of this country and the history of American medicine. In Germany in 1848 the two were scarcely more than boys, though they were acquitting themselves as men among men. We remember them first as associated with those stirring days. In Germany the exploits of Schurz, after the passing of well nigh ninety years, are legendary. He was 19 and Jacobi 18 at the time they enlisted in the cause of human freedom.

While Schurz escaped from the fortress of Rastatt in Baden after the disastrous battle there and found the means to liberate from Spandau his beloved teacher and friend, the scholar and leader, Gottfried Kinkel, many things were happening. Jacobi had enlisted as a surgeon in the medical corps of the revolutionary troops, fighting in Schleswig-Holstein, later to spend two years in a political prison. Schurz served as a lieutenant of the troops in the Palatine. Both were products of the liberal spirit that had swept their ancient and beloved University of Bonn. Coming to this country with the heritage and the remembrance of wonderful experience, they found very readily the places destined for the exercise of their genius and service, through many years of life, in the country of their affectionate adoption.

Schurz, still a youth in the days of the Lincoln campaign, found his place beside Lincoln himself and contributed greatly to the issue of that debate. He went to Spain as our first minister during the diplomatically troubled Civil War period.

He returned at his own urgent request to fight with the army; he gained a major-generalship and commanded a corps at Gettysburg. He became a senator from Missouri in 1869 and through the six years that followed was a joint leader with Sumner of liberal thought and action in Congress. In 1876 he was a cabinet minister; he was always "a maker of presidents" in the politics of his passing day. Later he was an editor of the New York Evening Post and of Harper's Weekly and president of the Civil Service Reform League. He was a never tiring commentator and adviser on everything in the current flow of public life—a great teacher as well as a great leader.

Jacobi passed rapidly through the many stages of his professional service, through the great posts of the hospitals and of the teaching platforms. He was president of the American Medical Association, president of your own fine, wonderful and useful body, which always was the "apple of his eye," and president of many another organization contributory to the main body of medicine, standing always forward in the many ways that have been so clearly outlined here today, so splendidly and so memorably oulined. Two such men, two such lives, indeed belong to the wealth of history.

I come to my simpler part. I think of them as first partners in an incomparable friendship, not as were even Damon and Pythias, but as far more. I doubt, indeed, whether any two men in the world ever felt more the loveliness of brotherhood—a brotherhood that found its beginnings in the old days at Bonn and on the battlefields of the great mid century revolution, to be strengthened through all the phases of their development and of their growth side by side in America. Not only their public life but their home life interblended, and their life here, through a long procession of beautiful and happy summers, interblended.

Schurz came to Lake George shortly after Jacobi did. The doctor first visited the lake in the year of the close of the Civil War, 1865. A short time later, in 1872, he bought these woodland properties. Twenty years after that two houses were built, the summer homes of Jacobi and Schurz. The doctor's house went down in flames, as you no doubt readily recall, in the year 1918. But the other still stands, in a sense a shrine, and a constant reminder of Schurz' spiritual presence here. They loved these woods and waters beyond anything that imagination can fancy. They brought to both a suggestion of the loveliness of the wooded places of their fatherland. Indeed, let us be assured that neither of them ever forgot the beauties of the Rhineland, just as neither ever failed to extol the wonderful literature of the lovely lyrics of Germany, though they became stalwart Americans.

When Schurz, having passed on, was spared the grief of the great struggle in arms which parted for a time nations that ever had been friends, and Jacobi, remaining, was called on to take his stand, need I say that he took it patriotically and promptly, lending his voice and his pen to the cause of his adopted land?

But here at the lake there was always calm. The two, with their families, lived here. It was not merely a matter of summer visitation. They both lived and worked here. Neither was ever idle. Here Schurz wrote the greater part of his Memoirs, which, sadly enough, were not completely finished; they were published with editorial assistance after his death. Likewise, the doctor had commenced the story of his life, the introductory chapters of which he read to his family and which, completed, would have been a wonderful legacy; but his manuscripts were lost in the fire, and he never found the heart to get back to the original composition that would have been required to restore them.

They lived and worked here, as I have said. But most of all they breathed the spirit of the lake and the spirit of each other. Schurz had his daily walk

along the 3 miles the doctor had carved in paths through the forest. The doctor had his. In the simplicity of their own terminology the members of the two households knew them as "the doctor" and "the General." The doctor carved the paths, and together they trod them and together loved them.

Schurz had names for the various points about the place that suggested to him old things or beautiful things or lovely things. Wagner contributed many of them. There were the "crags of the Walkyrie," the "Brunhilden rocks," the "springs of Bimini." This corner, which was one of the densest in the growth both of the trees and the glorious bloom beneath, was, as Dr. Shaw has said, the "Schwarzwald."

I was reminded the other day of how when Schurz, coming in from a walk, would mention airily one of these invented names of his, perhaps a new one, Mrs. McAneny or one of the others would say, "Where is that exactly?" and he would answer, "Why child, don't you know your own woods!" The names he had created belonged to him; he thought they belonged to others. I might add that they indeed grew to belong to his family and friends and that they will endure.

Then came the later years. It fell to the doctor to close the eyes of his friend, thirteen years before he himself passed on. These years of his own life were, however, years of great peace and serenity, little marred by real unhappiness or the dread of anything that life still might bring. There had begun to grow up about him five of his grandchildren. They were his comrades, and he adored them. In July of 1919, in his ninetieth year, he too died. He seemed rather to fade away than to fail. The burning of his house had indeed saddened him, for not only were his literary papers then lost but also practically all the contributory data, the notebooks and the private and professional histories he had been so long collecting. He told me then that he felt as though a part had been burned from out his life itself; and that year alone was not so joyous.

He died on a Thursday. On the Sunday preceding they brought from the village a little child, the grandson of Mr. Bixby, grievously ill. The child, carefully bundled, was carried to the doctor's house. He spent an hour over the boy, prescribed for him and directed the method of treatment; and I believe our chemist in the town still has that prescription, the last that Abraham Jacobi ever wrote, framed in his office. The child, in the judgment of its father, was perhaps saved that day. That was on Sunday. Then quickly came the doctor's own fast approaching end.

Although they were parted through these last years, I think to the doctor the presence of the general remained an actual part of his daily life. He always thought of him and often spoke of him. He remembered back and back across the years that had been so wonderful to both and which they had conspired constantly and beautifully to make memorable to all associated with them.

They left here in this village of Bolton a memory that in itself will always be bright. The doctor's interest in public affairs, exemplified in so many ways in broader fields, was quite as lively here in his summer home. The Lake George Association, which he helped to organize, and which is a sort of congress of the towns and villages scattered along these 35 miles of lake and mountains, drew much of his attention. He served as chairman of the first committee to check the pollution of the waters and of the first committee on the general public health of the countryside. His activities were irrepressible. The nearest thing was the thing that constantly called him, and to that nearest thing he always gave the best that he had to give.

So here too, while he "rested and worked," the welfare of his neighbors was always fresh in his mind. It seems part of the happy significance of this day that the time has come when this acre of the old wood, the gateway to the forest paths within, will actually be turned over to the immediate ownership and to the care and keeping of his fellow townsmen of Bolton.

The forests back of this spot, as I have said, are wondrously beautiful. They cover many broad acres, leading down to the shores of the lake. They are filled with glens and crags, groves of softly blended trees and vistas between that have their own rare loveliness. It has been the purpose of Mrs. McAneny, representing the doctor as she does today, that the woods should really be part of the park itself, freely open not only to the people of Bolton but to all those who come to visit here. It is, nevertheless, a matter of personal satisfaction to all Dr. Jacobi's family and friends that this acre, at the gateway, is to be separately and publicly owned, so that no change of time or circumstance can ever disturb it or mar the significance of your dedication.

It will remain, indeed, a hallowed place, well marked by the shining scroll you have placed upon this rock in the doctor's memory as well as by the bench of graven stone dedicated by the first Schurz committee to the memory of the General and now fittingly brought here so that they may stand together, a lasting reminder of the valiant lives of these two men, of their places in history and of the immortal quality of their friendship.

Mrs. McAneny has asked me to speak for her in the ceremony of turning over the deed of gift of the park to Mr. Vandenburg, president of our village board, who is here to receive it.

I feel there is nothing I might add to what I have said that might better express our satisfaction in being here today to perform this office. I shall ask Mrs. McAneny to hand to Mr. Vandenburg the "papers in the case."

(Mrs. McAneny presented to Mr. Vandenburg, president of the village board of Bolton Landing, the papers of deed.)

HONORABLE EDWARD M. VANDENBURG: It gives me great pleasure to accept this deed in behalf of the town of Bolton Landing. I also wish to say I am proud to be present at this great gathering in honor of such notable men. In the name of the people and the town of Bolton Landing, I thank you.

(The two papers which follow, read at the annual meeting of the American Pediatric Society at Bolton Landing on June 12, although not a part of the dedication exercises, contain interesting sidelights on the life of Dr. Jacobi. The first, a summary of the meeting of the society at Bolton Landing in 1905, was read by Linnaeus E. LaFetra, recorder and editor for the society at that time; the second, giving recollections of Dr. Jacobi, was read by Dr. Herbert Willy Meyer of New York.)

MR. LAFETRA: Thirty-one years ago, at the invitation of our first president, Dr. Abraham Jacobi, the seventeenth annual session of the American Pediatric Society was held at this place. Most of us arrived at Bolton Landing by lake steamer from Lake George. Of a total membership of fifty, twenty-nine were present at the meeting, and of these five are here today: Dr. Abt, Dr. Kerley, Dr. Morse, Dr. Shaw and I.

The sessions were held in the original Sagamore Hotel, burned some years ago, and in Dr. Jacobi's delightful home. A reading of the twenty-seven papers and of their discussion reveals much of interest and emphasizes the great advances

in knowledge during the years that have elapsed. The majority of the papers were of a clinical or pathologic nature, although some were related to laboratory studies, particularly of the urine and of the blood count in various conditions.

The president's address, delivered by Dr. C. G. Jennings, dealt with the comparatively new subject of the medical supervision of schools and school hygiene. Medical inspection of schools was established in Boston in 1894 and in New York in 1897. The meetings of those early days were generally enlivened by heated and acrimonious discussions of the feeding of infants.

The percentage method, so warmly advocated by Dr. Rotch, by which the fats, sugars and proteins could be changed quanitatively and relatively, was pitted against simple dilution of whole milk. Algebra was called in to aid in the construction of the baby's formula, and there was great debate over such formulas as 2-6-1 and 3-6-1.25. Calories as yet played little part in the calculations. Albumin milk and the different types of acid milks had not been developed.

Fig. 4.—The American Pediatric Society at its seventeenth annual session, at Bolton Landing in 1905.

Among the papers presented was one by Dr. Hara analyzing 145 cases of typhoid. How difficult it has been of recent years to show Stuart's examples of that disease in children.

Dr. Sanders made a plea for earlier intubation. At that time many pediatricians gained quite an income from practicing this procedure, but nowadays, with active immunization against diphtheria, which one owes to Dr. Schick, intubation is seldom needed. It would be interesting to know if any one here has performed an intubation in the past year.

Dr. Townsend presented a patient with intestinal and peritoneal tuberculosis. It is interesting that the tuberculin test was not used because the little patient had a constantly elevated temperature. This was before the introduction of the early skin test with tuberculin and of Calmette's conjunctival test, which was used with much misgiving and opposition.

The doctrine of allergy, with its multitudinous applications, was yet unknown in the study of pigment.

Scurvy was known to be due to a deficiency and to be cured by the ingestion of citrous juices, especially orange juice, but the vitamins had not been brought out by Funk.

Stenosis of the pylorus was a condition well recognized, but surgical treatment was still in the dark ages of gastro-enterostomy. The simple and safer method of slitting the tumor longitudinally, so successfully practiced by Downes and others, had not yet been devised.

New members elected were Drs. Howland, Southworth, Ruhräh and Knox. An honorary membership was accorded to Dr. Osler. It is interesting that the honored Sir William of later days had been the fourth president of our society in 1892.

The great charm of the meeting, of course, was Dr. Jacobi's warm-hearted and gracious hospitality. Even the humblest member, such as myself, was treated as an equal and welcome colleague. Dr. Jacobi was at his best when entertaining his pediatrician friends, either in his magnificent library on Thirty-Fourth Street, New York, opposite what is now Macy's, or in his country home.

We today are fortunate in being able to survey the many milestones of progress made since our last meeting here. When in another thirty years some of us return to this place, now hallowed for us as a shrine in honor of our first president, there will have been no doubt still greater advances.

May the American Pediatric Society continue to hold its place in the vanguard of pediatric progress!

DR. MEYER: When Dr. Shaw wrote to me some weeks ago and invited me to join in these ceremonies, I felt honored and elated that I could add my small share to the expression of love and admiration for our dear old man. I knew him well, for he was "Uncle Doctor" to us as children and he cared for us when we were ill. His kindliness and gentleness stand out in my memory with the impressiveness of childhood memories. It was partly due to him that my own father, Dr. Willy Meyer, came from Germany to our shores to live, and it was due to him that my mother and father settled on this blessed spot for their summers' rest.

The kindly smile, the gentle touch, the infinite kindness, the boundless knowledge, the persevering courage and the inspiring confidence are outstanding factors in the memory of Dr. Jacobi.

In 1865 Dr. Jacobi came to these shores of Lake George. For years he owned and lived on Hiawatha Island, just about one mile south of the Sagamore, and on that island his only son, Ernst, was born. Here he lived happily, and here he returned each summer until his son was stricken ill in the winter of 1883 with diphtheria. Dr. Jacobi had saved countless infants and children from the dread disease of those years, but, as happens so frequently in doctors' families, he was unable to save his own boy. Crushed, shaken and saddened, Dr. Jacobi did not want to come back to Lake George, and for some years his presence was sorely missed.

Then Carl Schurz and his family came to the Sagamore Hotel, in 1889 and 1890, and induced Dr. Jacobi to come with them. For several years these intimate friends and compatriots spent the summers together at the Sagamore.

Little wonder that these two great humanitarians loved Lake George! It is said that the famous Thomas Cook, who had traveled over the entire world, while sitting at a camp fire out in the far west was asked which lake of all he had seen in his travels he thought was the most beautiful lake in the world. He pondered a moment and then said, "Do you mean the grandest or the most

beautiful?" When his questioner said he had meant the most beautiful, Cook quickly and unhesitatingly answered, "Lake George." Of this fact Dr. Jacobi and Carl Schurz and all of us Lake Georgers were justly proud. Furthermore, it must not be forgotten that the waters of Lake George are the purest inland waters of any lake of its size in the civilized portions of this country. Dr. Jacobi, as chairman of the sanitation committee of the Lake George Association, helped to keep them so, and my late father, Dr. Willy Meyer, followed in his footsteps. Where the lake is from 25 to 30 feet deep on clear and quiet days one can see every stone and pebble on the bottom.

After Dr. Jacobi and his splendid and famous wife, Dr. Mary Putnam Jacobi, and Carl Schurz had been at the Sagamore for some years they decided to settle on some mainland property bought in 1875. This they did in 1892, building homes 2 miles north of here, at the spot where we are all going to assemble tomorrow to dedicate the park.

Dr. Jacobi built his own home and one for Carl Schurz, and later, after his only remaining child, his daughter Marjorie, married Mr. George McAneny and the little grandchildren came along, he built a third cottage, for them. How he loved, adored and worshiped those grandchildren!

Dr. Jacobi was kind and so good and self-sacrificing. As the dust of the busy road of life settled on his wonderful leonine head he became constantly more mellow, softer and gentler. I well remember one day some thirty years ago, when he was already in his seventies, that there was a terrific north gale on the lake. Many of the neighbors were down on the dock watching the wild waves break over the pier, when suddenly, far off to the south, a little boat was spied. Who could it be who dared to risk his life out in this raging sea? All that could be seen was the spray of the waves as they pounded on the boat. As the boat came nearer it finally became apparent that it was the old gentleman, all alone in his boat, the Hiawatha. Let it not be forgotten that he was then almost eighty years old. Why was he out on that wild lake? Duty—his indomitable sense of duty. There was a sick patient in Kattskill Bay, 8 miles south, whom he had promised to see, with the local doctor, and storm or no storm Dr. Jacobi went, and God took care of him and brought him to a safe return.

As Dr. Jacobi grew older he worked harder and more steadily on his autobiography. Just think of his experiences—his youth in revolutionary Germany in 1848, his early medical career in America, when medicine and surgery were developing, his skyrocketing up and up as a pioneer in medicine, his founding of the specialty of pediatrics in America and, at the age of 84, the zenith, his election to the presidency of the American Medical Association. He was always fearless and in the vanguard of progress.

One cold night in September when he was 88 years old, he sat before the fire in his cottage at Lake George, reading chapters of his biography to his daughter, Marjorie. As he finished the fire was dying down, and they both retired, he in his own home alone and his daughter to her home. Some hours later he awakened and heard a loud crackling sound; he opened his door and found the living room in flames. He slammed the door and rushed to the window; it was locked, and he could not open it. He broke the window with his elbow and let himself drop about 10 feet to the ground. Marjorie McAneny and others found him sitting on the ground bewildered and stunned, watching his beloved home burn down, and with it his autobiography. There was no copy. To a man 88 years of age this

was a crushing blow. For a few days he stayed at my home here on the island; then he went to the Schurz cottage, and finally, to the city. He did not have the enthusiasm to start work on his autobiography anew.

The following summer he returned to Lake George and lived in the middle Schurz cottage. His friend Carl Schurz had died some years previously, and things were not the same. The spot where once had stood his home was bare; his autobiography was gone; the advancing years made an abyss in his life. My father and I called on him once that summer, and there he sat, alone on his porch, looking out over the mountains and lake and woods he loved so dearly. Life and strength were ebbing; the fire had been a terrific blow. One day shortly thereafter Mrs. McAneny called my father to come and see him. He was not well; slowly his staunch heart was failing. The following day, with my father and his daughter with him, his worldly life ceased.

But Dr. Jacobi lives on, and that is why we are assembled here today, eighteen years later, to honor and revere his memory and to pay our devoted homage.

News and Comment

GENERAL

Pediatric Number of the Chinese Medical Journal.—*The Chinese Medical Journal*, the official organ of the medical profession in China, published at Shanghai, devoted the April number to pediatrics in China. The number is about twice the usual size and contains original articles, clinical reports and discussions, topics of special interest, statistics and surveys, addresses and reviews, articles on hygiene and public health, clinical notes and memoranda and much other material. The editorial is on the "National Children's Year" which is being celebrated throughout China in 1936. Dr. H. H. Kung, president of the National Child Welfare Association in China, states that "there is no country today that does not realize the importance of child welfare, for the intelligence and good citizenship of the youths of today are measured by the amount of energy and time that is spent on their education and welfare when they are children, and no modern nation can afford to overlook this fact." China is following the encouraging example particularly of Great Britain and New Zealand in the effort to reduce the high infant mortality.

The activities of the National Child Welfare Association in China and other social work for children are described in this number of *The Chinese Medical Journal*. The scientific communications have been abstracted and will be found in subsequent numbers of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

American Board of Internal Medicine.—The American Board of Internal Medicine, composed of the following physicians, has been organized: Walter L. Bierring, Des Moines, Iowa, chairman; Jonathan C. Meakins, Montreal, Canada, vice chairman; David P. Barr, St. Louis; Reginald Fitz, Boston; Ernest E. Irons, Chicago; William S. Middleton, Madison, Wis.; John H. Musser, New Orleans, and G. Gill Richards, Salt Lake City.

Further information may be obtained from the secretary, Dr. O. H. Perry Pepper, Philadelphia.

Examinations of the American Board of Pediatrics.—Examinations will be held by the American Board of Pediatrics as follows: on Thursday, October 22, at San Francisco, preceding the meeting of Region IV of the American Academy of Pediatrics; on Sunday, November 15, at Baltimore, preceding the joint meeting of Regions I and II of the American Academy of Pediatrics with the Southern Medical Association, and on Thursday, November 19, at Cincinnati, preceding the meeting of Region III of the American Academy of Pediatrics.

Talks by Radio on Growth and Development of the Child.—The National Congress of Parents and Teachers, with the American Academy of Pediatrics and the National Broadcasting Company, is presenting over the radio a series of thirty talks on the growth and development of the child. A talk is to be given each Wednesday afternoon from 4 to 4:30, eastern standard time, over the NBC-WJZ Blue Network, from Oct. 21, 1936, to and including May 19, 1937.

The speakers include the outstanding investigators in pediatrics in the United States.

Fourth International Pediatric Congress.—The Fourth International Pediatric Congress has been definitely set for Sept. 28, 29 and 30, 1937, at Rome, Italy. It will be followed immediately by the Second International Congress for the Protection of Infancy.

International Congress of Pediatrics.—The International Congress of Pediatrics has again been postponed; it will convene in September 1937.

UNIVERSITY NEWS

The meeting of the University of Michigan Pediatric and Infectious Disease Society has been postponed until October 30 and 31.

PERSONAL

Dr. Clifford G. Grulee, Evanston, Ill., has been elected a corresponding associate of the Cuban Pediatric Society.

DEATHS

On May 4, 1936, Dr. David Greig of Edinburgh, Scotland, died. He was 72 years old. Through a long and constantly active professional life, he had written regularly and interestingly on anatomic and pathologic subjects, especially congenital malformations. Most of his writings may be found in the *Edinburgh Medical Journal*. His active career of writing dates from 1893 to the year 1935, when he published three articles in that journal.

His work is of particular interest to pediatricians because of his experience with mentally deficient children. Since he was an anatomist as well as a surgeon and a clinician, his descriptions gave detailed information of anatomical abnormalities. This is notably true of his work on mongolism. Soon after the World War he accepted a directorship of the Museum of the Royal College of Surgeons at Edinburgh, which is connected with the medical school there.

His death is a loss to the medical profession because of his continued activity and scientific productions. His one hundred and forty printed contributions will remain an authoritative source in fields which had not previously been extensively covered. They might well be republished in a special volume to his memory.

Dr. Charles Schott of Chicago, who was for many years an attending pediatrician at the Children's Memorial Hospital, died on October 1, at the age of 51 years. Dr. Schott had been especially interested in the child welfare activities of the American Legion in the State of Illinois and was a former president of the Chicago Pediatric Society.

Dr. N. N. Allen of Houston, Texas, died on September 22 in an attack of angina pectoris. Dr. Allen was one of the oldest and certainly one of the best loved pediatricians in Texas. He was the first man in Houston to devote his time exclusively to pediatrics and was always known there as a friend of the younger pediatricians. Both as a doctor and as a man, Dr. Allen will be deeply missed.

Dr. Egon Helmreich, chief of the children's section of the Kaiser-Franz-Joseph Spital, Vienna, Austria, died on August 24, at the age of 44 years.

Dr. Helmreich's work on the physiology of infancy is well known. He made many other outstanding contributions, and his loss will be felt.

Abstracts from Current Literature

Anatomy and Physiology

THE EFFECTS OF OESTRIN ON THE UROGENITAL TRACT OF THE MALE MONKEY. G. VAN WAGENEN, Anat. Rec. **63**:387 (Nov. 25) 1935.

Theelin caused hyperplasia of the fibromuscular stroma of the seminal vesicles and prostate of the macaque monkey. It changed the epithelium of the urethra, prostatic utricle and seminal vesicle from the cuboidal type to the keratinizing type similar to that seen in the vagina. SNELLING, Toronto, Canada.

METABOLISM OF WOMEN DURING THE REPRODUCTIVE CYCLE: VI. A CASE STUDY OF THE CONTINUOUS NITROGEN UTILIZATION OF A MULTIPARA DURING PREGNANCY, PARTURITION, PUERPERIUM AND LACTATION. HELEN A. HUNSCHER and others, J. Nutrition **10**:579 (Dec.) 1935.

The authors have previously emphasized that data from many other studies of metabolic processes of healthy, pregnant, nonpregnant, lactating and postlactating women should not be regarded as constants peculiar to a given stage of reproduction of women in general, because data accumulated over brief intervals or periods may be affected by various factors which do not lend themselves to control.

In the present study these workers were fortunate in being able to observe the reproductive cycle of a healthy woman for a period of twenty-one weeks of gestation through delivery and the puerperium to the eighth week post partum. The results of their observations may best be presented by their summary, which is as follows:

"A case study extending over an 8-year period of child bearing and child rearing has been made on a woman when she and her children were known to enjoy buoyant health.

"Uninterrupted nitrogen metabolic responses during the last half of fetal development and the physiological preparation of the maternal body for lactation and the extension of these observations into parturition, puerperium and 8 weeks of lactation showed where some of the stresses and strains of maternity lay. The results confirm previous considerations derived from intermittent balances in two former reproductive cycles in the same woman.

"During the last 145 days in gestation there was an average net storage of 3.1 Gm. and a maternal retention of 2.6 Gm. of nitrogen daily resulting in a total observed accumulation of 446 Gm. at term.

"On the day of delivery the chemically determined maternal loss in blood, placenta, amniotic fluid and vomitus amounted to loss from the body beyond the food consumed amounted to 54.6 Gm. of nitrogen in addition to that contained in the fetus.

"The nine daily balances during the lying-in period showed an average daily loss of 0.87 Gm. of nitrogen.

"By the fifty-third day of milk flow the gestatory reserve nitrogen had been reduced by delivery, puerperium and lactation losses of 54.6, 44.6 and 38.3, respectively, leaving a total of 310 Gm. of nitrogen stored only in the last half of pregnancy. When the approximate fetal content of 58.6 Gm. of nitrogen is deducted from the final maternal reserve, the accountable losses of the reproductive cycle by the fifty-third day of lactation had left a maternal reserve of 250 Gm. of nitrogen for future dissipation or enrichment of the maternal body at termination of the reproductive cycle." MUNNS, Winnetka, Ill.

Respiratory and Vascular Changes in the Mammal Before and After Birth. Joseph Barcroft, Lancet **2**:647 (Sept. 21) 1935.

The information was procured mostly from experiments on sheep and goats which were subjected to cesarean section.

In attempting to determine what proportion of the whole fetal blood was actually in the fetus and what proportion in the placenta and cord it was found that the former contained from one half to three fourths of the blood and the latter from one fourth to one half. There is reason to believe that the blood from the placenta, or most of it, is withdrawn into the fetus at birth.

Barcroft proved that oxygen want is the essential cause of the first breath. He produced anoxemia by turning a portion of the fetal hemoglobin into methemoglobin. This he did both by the injection of hydroxylamine chloride and potassium ferricyanide. The respiratory movements thus produced were again abolished by the injection of blood into the fetal circulation.

In regard to the course of the fetal circulation the findings in summary are the following:

1. The blood which passes through the heart may be regarded as forming two streams approximately equal in volume.

2. One of these goes to the head and is not much inferior in its oxygen content to the redder blood which reaches the heart, namely, that coming along the inferior vena cava.

3. The second, which is not much redder than the venous blood from the head, goes to the body, which means the lower part of the trunk and the placenta.

The fetus possesses a hemoglobin of a different type from that of the mother, a hemoglobin with a higher affinity for oxygen; this is true of the goat, the sheep and the rabbit. The hemoglobin of the human fetus and even of the new-born child has less affinity for oxygen than that of its mother, but this anomaly is set right when the hemoglobin is not in solution but in corpuscles. It happens that in the same buffer solution and at the same temperature the fetal corpuscles in man, as in other animals, have a greater affinity for oxygen than those of the mother.

Langmann, New York.

The Lung Volume of Normal Children. E. Püschel, Monatschr. f. Kinderh. **63**:450, 1935.

Studies of the vital capacity were made on fifty-two healthy girls and thirty healthy boys. The children were divided into three groups—school girls, girl patients in a clinic and school boys. There was little difference in the three groups. In an analysis of the different components of the respired air as regards volume, the boys gave results identical to those reported for adults. In other words, the proportion of residual air, tidal air and supplemental and complemental air remain relatively constant.

Gerstley, Chicago.

Biochemistry, Bacteriology and Pathology

Pathologic and Immunologic Problems in the Virus Field. Thomas M. Rivers, Am. J. M. Sc. **190**:435 (Oct.) 1935.

This article is well worth reading in the original. It is concluded that there is no definite reason as yet to believe that the general principles of immunity, many of which are not known or understood, fail to operate in the field of viruses. Most of the immunologic and serologic oddities encountered in this domain apparently can be accounted for either by the intimate type of parasitism exhibited by the viruses or by the multiplicity and lability of antigens involved.

Henske, Omaha.

PROPAGATION OF THE VIRUS OF EPIDEMIC INFLUENZA ON THE DEVELOPING EGG. F. M. BURNET, M. J. Australia **2**:687 (Nov. 16) 1935.

The virus of epidemic influenza has been propagated for fourteen generations on the chorio-allantoic membrane of the developing egg. Characteristic lesions are produced. The method may serve as a useful means of preparing antigens for immunization against influenza.

GONCE, Madison, Wis.

ARE SERUM PROTEINS AFFECTED BY THE TIME THE BLOOD STANDS BEFORE REMOVING THE SERUM FROM THE COAGULATE? JENS BING, Acta med. Scandinav. **86**:367, 1935.

Bing found in four normal patients and in one patient with nephrosis that the values for the total protein content and those for the albumin-globulin ratio were not altered after the samples of blood were allowed to stand four hours.

KAJDI, Baltimore.

Metabolism; Infant Feeding; Milk and Other Foods

BREAST AND ARTIFICIALLY FED INFANTS. C. G. GRULEE, H. N. SANFORD and H. SCHWARTZ, J. A. M. A. **104**:1986 (June 1) 1935.

In all types of feeding the morbidity from infection increases each month until the fifth month. In the breast-fed and the partially breast-fed infant there is then a decrease, which continues through the ninth month. In the artificially fed baby the morbidity from infection increases through the ninth month. The breast-fed baby is practically free from gastro-intestinal disorders. These disorders increase to the fifth month in infants who are partially breast fed and increase to the seventh month in artificially fed infants. From the curves for mortality, the breast-fed baby appears to be in danger only in the first month, while the greatly increased mortality of the artificially fed babies in all months is evident. The authors summarize their study of 20,000 infants by stating that there is a definite rise in the morbidity in artificially fed infants, a rise not shared in by the breast-fed or partially breast-fed group, and that the mortality for the breast-fed infant occurs almost entirely in the first two months of life.

BONAR, Salt Lake City.

THE NUTRITIVE VALUE OF ANIMAL TISSUES IN GROWTH, REPRODUCTION AND LACTATION: III. THE NUTRITIVE VALUE OF BEEF HEART, KIDNEY, ROUND AND LIVER AFTER HEATING AND AFTER ALCOHOL EXTRACTION. WALTER H. SEEGERS and H. A. MATTILL, J. Nutrition **10**:271 (Sept.) 1935.

Rats grew poorly on rations of liver extracted with alcohol. Those given other meats extracted with alcohol were but slightly retarded in growth. Similar results were obtained when heat-treated meats were used. Apparently the protein of liver is peculiarly sensitive to alteration by heat and by hot alcohol. The decreased nutritive value of the other meats may be due solely to a loss of their accessories in the process by extraction of alcohol. Liver suffers both a loss of accessories and an alteration of protein.

MUNNS, Winnetka, Ill.

A STUDY OF IRON METABOLISM WITH PRESCHOOL CHILDREN. LEAH ASCHAM, J. Nutrition **10**:337 (Sept.) 1935.

Previous work by different investigators had indicated rather divergent figures for iron requirements in young children. One group believed that 0.6 mg. per kilogram of body weight is necessary to meet the needs of growth and maintenance in preschool children. Another group considered 0.48 mg. adequate. The author, working with six subjects, two girls and four boys, aged from 4 to 6 years, under conditions apparently well controlled, found that the retention of

iron varied from 0.01 to 0.15 mg. per kilogram with intakes of from 0.55 to 0.64 mg. per kilogram. Averages were 0.07 mg. and 0.59 mg., respectively.

MUNNS, Winnetka, Ill.

INSULIN IN THE MALNUTRITION OF NONDIABETIC CHILDREN. ABRAHAM TOW, New York State J. Med. **35**:719 (July 15) 1935.

Twenty-seven children with malnutrition were hospitalized and after a preliminary blood sugar estimation was made were given 5 units of insulin twenty minutes before each meal. The appetites increased immediately, and twenty-four gained from 1 to 3 pounds (0.5 to 1.3 Kg.) per week; only three failed to make a satisfactory gain. No unfavorable reactions occurred. There was a loss of weight in several cases when insulin was discontinued.

AIKMAN, ROCHESTER, N. Y.

WHEN IS FOOD TOXIC? C. ULYSSES MOORE, Northwest Med. **34**:196 (June) 1935.

Moore contrasts the improvement in the morbidity and mortality of infants and children with the morbidity and mortality of the 40 year old patient. Of eight infants born alive, at the age of 40 only two will be able-bodied; three will be supported by these two, and the rest will be dead. The author quotes McCollum, who stated that the chief factor in disease lies in the unwise choice of foods.

The principal faults in the average diet are lack of vitamins, an unbalanced proportion of acid and alkaline ash foods, lack of minerals and deficiency of adequate protein.

Another source of disability arises because of individual sensitivity to foods. Moore believes that about 20 per cent of persons are allergic and exhibit difficulties in the handling of one or more foods. After the age of 40, gastrointestinal allergy becomes increasingly frequent.

The caloric radiation decreases from 40 calories per hour per square meter of body surface at 17 years to 35 calories at 38 years and to 28 calories at 60 years. This calls for a regulation of diet as a person grows older, a regulation which may not occur by natural decrease of appetite

SCOTT, Philadelphia.

THE DEBILITATED CHILD. W. E. SNELL, Brit. J. Phys. Med. **9**:181 (Feb.) 1935.

The hereditary and environmental factors which have to do with growth and development are considered. Diet is said to be the most important. The use of the "faddy" type of diet which contains large quantities of residue-producing food such as brown bread, cereals and fruit is deplored. Clothing and psychologic factors are discussed. Wholesale tonsillectomies are deplored. Recurrent bronchitis is said to be the most common type of respiratory infection in these children "who are always ailing but never ill." Tuberculosis, subacute rheumatism and urinary infections are mentioned.

HARTMAN, Cleveland.

THE SITE OF FORMATION OF THE PHOSPHATASE OF SERUM. A. R. ARMSTRONG and F. G. BANTING, Canad. M. A. J. **33**:243 (Sept.) 1935.

The purpose of this paper was to report certain experiments which were carried out to ascertain the tissues of the body which are responsible for the formation of tissue phosphatase.

In the following organs, which were removed from different dogs, the serum phosphatase content was assayed before and after removal: the small intestine, the large intestine, the kidneys, spleen, pancreas, liver, testes and epididymitides and all the abdominal viscera except the adrenals and the bladder. In no case did the serum phosphatase content decrease, but frequently an increase took place. This was taken as evidence that these organs do not control significantly the formation of this enzyme in the serum. These observations support the contention that bone is the sole source of serum phosphatase.

MOORE, Omaha

INFLUENCE OF CEREALS ON CALCIUM, MAGNESIUM AND PHOSPHORUS ASSIMILATION. S. RANGANATHAN, Indian J. M. Research **23**:229 (July) 1935.

Rats were put on a diet of whole wheat, cambu cake, cholam cake, raji cake and polished rice flour. Calcium was assimilated best with a diet of whole wheat, cholam and polished rice. Magnesium was assimilated best with a diet of whole wheat and polished rice. All the diets allowed but poor growth.

SNELLING, Toronto, Canada.

THE "DIGESTIBILITY" OF COMMON FOODSTUFFS AS DETERMINED BY RADIOGRAPHY. W. C. MAILE and K. J. L. SCOTT, Lancet **1**:1500 (June 29) 1935.

Simple boiling of milk is the only one of the usual methods employed to increase the digestibility which has much effect in reducing the emptying time of the stomach. The child's stomach deals with milk relatively more quickly than that of the adult and with sugar more slowly. Sugar is much more rapidly absorbed from the stomach when fluid is drunk with it. The taking of fluids after meals materially hastens the passage of food through the stomach.

LANGMANN, New York.

THE ARTIFICIAL FEEDING OF INFANTS. WILFRED SHELDON, Practitioner **134**:415 (April) 1935.

Failures in feeding formulas are due more often to an incorrect amount of food (usually underfeeding) or to simple errors in the technic of feeding than to an unsuitable formula. A thorough discussion of the basic principles of infant feeding is presented before the author considers the composition of cow's milk and the various ways of using it. The general consideration of the amount of food required, the times of feeding, the dilution of milk, the addition of sugar and the addition or reduction of fat, as well as the protein requirement, gives a good review of the fundamentals of infant feeding.

The proprietary infant foods are presented under the main divisions of dried milk, condensed or evaporated milk and food (mainly starchy) intended only as additions to milk. Iron and vitamin needs are also discussed.

SAPPINGTON, San Francisco.

THE ADVANTAGES OF BREAST FEEDING. CLIFFORD G. GRULEE, Bull. Assoc. internat. de pédiat. prevent. **2**:3, 1935.

The Infant Welfare Society of Chicago, founded twenty-five years ago, with stations in the poorest sections of the city and affording service to children of many nationalities, conducted an inquiry continuing from 1924 to 1929 into the relative values of breast milk and artificial feeding.

In this survey no less than 20,061 infants were studied. These were followed for a period of nine months, with weekly visits of the visiting nurse following a thorough preliminary examination. Comprehensive tables supply information concerning the morbidity and mortality of this large group, of which 9,749, or 48.5 per cent, were entirely breast fed with accessory feeding added; 8,605, or 43 per cent, were partially breast fed, and 1,707, or 8.5 per cent, were fed artificially.

The morbidity rate was notably higher in the two latter groups. The death rates in the three categories were even more striking: The mortality among those fed exclusively from the breast was 1.1 per thousand; in the partially breast fed it was five times as high, and in those artificially nourished it was almost ten times greater.

AMESSE, Denver.

BUTTERMILK IN INFANT FEEDING. DENISE ROUGET, Bull. méd. de hôp. Bretonneau, 1935, p. 514.

Buttermilk is indicated for feeble infants, for the new-born, for those with whom cow's milk disagrees and for those who vomit because of stasis. In the

latter about two thirds of the contents of the stomach pass the pylorus; then a sudden stoppage occurs. Three hours later the contents of the stomach still amount to 15 or 20 cc., and the increased total acidity indicates considerable lack of hydrochloric acid. Antispasmodics are without effect, and cereals are not well tolerated. In three reported cases buttermilk was the only nourishment which checked the vomiting and loss of weight. Buttermilk is also indicated in eczema, prurigo, hypothrepsia and acute putrefactive dysentery.

VINTON, New York.

HEMOSTATIC ACTION OF HUMAN MILK. L. LINDENFIELD, Presse méd. **43**:1332 (Aug. 24) 1935.

Lindenfield found that the addition of human milk to venous blood accelerates clotting by as much as twenty times the normal time. He cites an example in which clotting of blood alone took place in nine hundred seconds; with the addition of human milk in forty-nine seconds. Cow's milk is less efficacious than human milk. This coagulating power does not extend to oxalated or citrated plasma, but when blood treated with oxalates or citrates has been recalcified the acceleration in the clotting time is marked. By mixing human milk with isolated prothrombin and calcium chloride and heating to 37 C., active thrombin may be formed; this thrombin (oxalated to exclude the influence of the calcium) demonstrates on decalcified plasma a marked coagulating power. This seems to the author conclusive proof that human milk acts as a cytozyme (or thrombokinase).

Clinical evidence of the coagulating power of human milk is sparse, but in three cases of prostatectomy it was used with apparently splendid results. The author admits that the problem of hemorrhage is not identical with that of coagulation but believes that in capillary hemorrhage the rôle of coagulation is a major one.

BIEKER, St. Petersburg.

MALT. RENÉ MATHIEU, Rev. franç. de puériculture **3**:36, 1935.

In selecting a malt product for infant feeding one should consider whether it contains: (1) soluble starch, dextrins and maltose and in what proportions; (2) active ferments capable of transforming starch to soluble starch or dextrin-maltose and (3) vitamin B. The type of malt to be selected will depend on whether the infant is normal or suffering from some nutritional disturbance. The merits of various commercial products are discussed.

CRANE, Chicago.

EXPERIMENTAL STUDY OF VARIATIONS IN THE WATER CONTENT IN EARLY INFANCY IN NORMAL AND PATHOLOGIC CONDITIONS. MANLIO GUZZINI, Fisiol. e med. **5**:601 (Aug. 20) 1934.

Studies of more than fifty children, both new-born and prematurely born, in the first few years of life showed that the fluidity of the blood diminishes immediately after birth, then increases with daily oscillations during the period of nursing. In exudative, pasty children it has a tendency to increase, while in those whose blood is less fluid it tends to diminish.

VINTON, New York.

LIPEMIA, AMINO-ACIDEMIA AND GLYCEMIA DURING DIGESTION IN HEALTHY AND IN ATHREPTIC INFANTS. P. SCHIAPARELLI, Riv. di clin. pediat. **33**:946 (Aug.) 1935.

Schiaparelli reports an increase in the amino-acid content and the sugar content of the blood following feeding in both the breast-fed and the artificially fed healthy infant. The athreptic infant showed a similar increase during digestion.

In the normal infant there was an increase of the total fat content of the blood following the taking of food. The maximum increase was reached two

hours after the meal in the breast-fed infant and three hours after the meal in the bottle-fed infant. One hour after the meal there was occasionally hypolipemia.

The athreptic infant showed hyperlipemia before feeding, which developed into hypolipemia during the digestion of food. HIGGINS, Boston.

THE ALKALI RESERVE IN CHILDHOOD. ISIDORO GIUZIO, Arch. de pediat., Rio de Janeiro **7**:585 (July) 1935.

This article takes up the entire issue. The author estimated the alkali reserve on groups of children consisting of from ten to fifteen members in each group, from the new-born period to puberty. He varied this by studies on temperature, sex, humidity and diet. This article cannot well be abstracted but should be read in full by any one interested, as it should set a standard for these values at all ages in childhood. SANFORD, Chicago.

INFANT FEEDING. SALOMAO CRUZ and EDUARDO DE CARVALHO, Arch. de pediat., Rio de Janeiro **7**:673 (Aug.) 1935.

Various problems of infant feeding are discussed. Milk, to be satisfactory, must be well pasteurized and transported properly. If it is deficient in vitamins they must be supplied. Medicinal milks should be used only in cases of the specific conditions for which they are of service. SANFORD, Chicago.

MEAT IN THE DIET OF INFANTS. D. GUILLERMO ANGULO PASTOR, Puericult. españ. **5**:8 (Aug.) 1935.

In a survey it was found that the time for starting meat in the diet varied from five months (Knauer) to five years (Tailleus) and that a majority of authors agreed on the following points: (1) At about 15 months of age, meat products which do not require mastication—beef broth, meat reduced to a pulp and beef juice—may be given. (2) At about 20 months of age, when the infant has sixteen teeth, tender meat in very small pieces may be given. These regimens exclude extremes and employ a diet rich in meat and poor in milk; they are used on a large scale by the Germans, who for several years have been studying diets without milk.

Hamburger has proposed as a basis of amino-acids, minerals and vitamins for children with intolerance to milk, elimination of milk and its prolonged substitution by a pap deriving its protein from calf's liver cooked and triturated in a mortar, in doses of from 40 to 80 Gm. Knauer, of Breslau, at the end of the fifth month, substitutes for one or two nursings, as an antirachitic, paps with meat. These paps are prepared with broth from bones and calve's liver in which are cooked various vegetables, grits and rice and to which is added a large tablespoonful of meat pulp.

This regimen without meat is indicated in cases of eczema, tetany and intolerance to milk in severe cases of dyspepsia and in cases of anorexia, vomiting, rickets, alimentary anemia and other conditions. GIFFEN, Toledo, Ohio.

QUANTITY OF PROTEIN IN ALBUMIN MILK. FLORENCIO ESCARDÓ, Semana méd. **1**:22, 1935.

Although, theoretically, albumin milk made as originally described by Finkelstein should contain 20 Gm. of casein to each liter of milk, which, added to the casein of the original, makes a total of 5.5 per cent, the author found this content to vary greatly (from 3.18 to 5.73 per cent). The variation was no doubt due to the season of the year and the breed of cattle.

SANFORD, Chicago.

PATHOLOGY OF DYSTROPHY IN INFANTS. ZOLTÁN VON GULÁCSY, Arch. f. Kinderh. **105**:43, 1935.

Study of the nitrogen metabolism in dystrophic infants indicated that the dystrophy affects the entire organism and that the liver is the chief point of attack. The degree of the lesion is proportional to that of the dystrophy. The critical point in the ability to react is when the infant is from 30 to 40 per cent underweight. The figures for the nitrogen metabolism should be reckoned on the basis of the desired body weight.

CRANE, Chicago.

ESSENTIAL ACETONEMIA IN CHILDREN. H. J. SPÖRL, München. med. Wchnschr. **82**:1275 (Aug. 9) 1935.

The symptomatic acetonemia associated with diabetes, infections and starvation is well known. Essential acetonemia occurs in cyclic vomiting. In children with cyclic vomiting acetone is found in the urine at the beginning of the attack, i. e., not as a result of the vomiting or starvation. Spörl reports several cases with a different clinical picture associated with essential acetonemia. The illness that he observed differed from cyclic vomiting in that it did not recur; the vomiting was a less prominent symptom, and the cerebral manifestations were more pronounced. The cerebral manifestations varied from confusion to stupor, and in some cases there were convulsions. The acute symptoms subsided in a day or two, and complete recovery was rapid. The treatment is the same as that for cyclic vomiting, namely, the administration of dextrose.

BRAHDY, Mount Vernon, N. Y.

HORMONE THERAPY OF ATHREPSIA IN INFANTS. P. ROBOZ, Orvosi hetil. **79**:467 (April 27) 1935.

Roboz gave thymus extract to infants in doses of from 0.5 to 1 Gm. per kilogram of body weight. This therapy is totally harmless. Recovery occurred in six, and improvement in eight of the twenty cases observed by the author.

GÖTTCHE, Budapest, Hungary.

Vitamins; Avitaminoses

THE SIZE AND STRUCTURE OF THE THYROID GLAND OF THE CAT AFTER THE ADMINISTRATION OF IRRADIATED ERGOSTEROL. A. M. LANDS and O. O. STOLAND, Endocrinology **19**:701 (Nov.-Dec.) 1935.

Seasonal changes in the structure of the thyroid gland, consisting of hyperplasia occurring during winter months, have been described. The fact that the thyroid gland is found to be in the colloid or "resting" state during the summer months, when there is a high ultraviolet ray content in the sunlight, suggests that these changes may result from the greater amount of viosterol available at this season.

In the present investigation, the effect of various levels of intake of viosterol on the size and structure of the thyroid gland was studied.

The administration of nontoxic amounts of viosterol to young cats caused no significant alterations in the normal structure of the thyroid gland. The administration of toxic amounts resulted in marked microscopic alterations in the structure of the thyroid. Whereas in the normal gland the vesicles were small or collapsed, after the administration of toxic amounts the vesicles were large and the colloid abundant. Some difficulties in attributing this change to a direct action of viosterol are pointed out.

JACOBSEN, Buffalo.

CHEMISTRY OF VITAMINS. J. C. FORBES, South. M. J. **28**:839 (Sept.) 1935.

Great strides have been made in determining the chemical structure of vitamins, as well as the mechanism of their physiologic actions. Little is known regarding the mechanism of the action of vitamins A, B_4 and E. Vitamins B_1, B_2 and C

seem to be involved in oxidation processes. Vitamin B_1 possibly acts as a co-enzyme to a dehydrogenase, while vitamin B_2 is an important constituent of the "yellow oxidation ferment" of Warburg and Christian. Vitamin C, through its ability to undergo reversible oxidation, probably acts as an oxygen carrier in cellular metabolism. Vitamin D influences the calcium and the phosphorus metabolism possibly acting primarily by diminishing the intestinal excretion of calcium.

SCHLUTZ, Chicago.

DEGREE OF ANTISCORBUTIC ACTIVITY OF ASCORBIC ACID. LUCIE RANDOIN, Compt. rend. Soc. de biol. **116**:4, 1934.

Guinea-pigs weighing from 430 to 630 Gm. were divided into groups and fed a scorbutic diet. One group was a control. Cevitamic acid was added to the diet of the others in daily doses of 0.05, 0.1, 0.5, 0.75 and 1 mg., respectively.

Scurvy developed in the groups that received 0.05 and 0.1 mg., as well as in the controls. All the other groups were protected.

It is noted, therefore, that larger amounts (more than 0.1 mg.) of cevitamic acid are necessary to prevent avitaminosis, as compared to 0.005 mg. of carotene and 0.0005 mg. of irradiated ergosterol necessary to prevent avitaminosis A and D, respectively.

WAHL, Cleveland.

SYNTHESIS OF VITAMIN C IN INFANTS. P. ROHMER, N. BEZSSONOFF and E. STOERR, Nourrisson **22**:286 (Sept.) 1934.

With the use of the mono-molybdophosphotungstic acid test for determination of the presence of vitamin C in the urine, experiments were made on infants of different ages with diets containing and diets lacking vitamin C. Infants from birth to the age of 9 months were able to synthesize their own supply of vitamin C, even when they were fed a diet lacking this vitamin. In infants between 9 and 11 months of age this ability varied, while it disappeared entirely in the infants of more than 1 year. From this observation it follows that the addition of vitamin C to the diet is necessary only for infants over 6 months of age. This statement applies to healthy infants. Studies are being made to determine the effect of infections and other pathologic processes on the power of young infants to synthesize vitamin C.

MCCLELLAND, Cleveland.

RICKETS: ITS TREATMENT AND PROPHYLAXIS. A. B. MARFAN, Rev. franç. de puériculture **3**:3, 1935.

The benefits obtained from the various methods of treating rickets are compared. Preference is given to the ultraviolet rays or irradiated ergosterol in courses of about twenty days each, separated by intervals of about fifteen days. Meanwhile any underlying condition such as syphilis or other chronic infection must receive appropriate care. Recommended for prophylaxis are: exposure to the sun's rays when possible; treatment with the ultraviolet rays during the winter (two series of ten exposures each), or the administration for from ten to fifteen days of each month of 10 drops of an oily solution of ergosterol or of 1 teaspoonful of cod liver oil.

CRANE, Chicago.

THE CEVITAMIC ACID CONTENT OF THE RETINA AND ADRENALS OF ANIMALS. H. BRACCI-TORSI, Arch. di ottal. **42**:80 (March-April) 1935.

The method of Harris and Ray was employed, with a number of additional precautions to insure accuracy. By bubbling carbon dioxide through the solutions before testing them the very rapid reduction of cevitamic acid (introduced as ascorbic acid) which occurs without this procedure is reduced to the minimum,

and this is advised whenever a solution cannot be tested immediately. The retina and adrenals of beef and swine were employed, the amount of cevitamic acid per gram of fresh tissue being estimated.

For young cattle from 1½ to 3½ years of age the amount in the retina varied from 0.11 to 0.17 mg. per gram, the average being 0.14 mg. The amount in the adrenals averaged 1.1 mg. per gram. In cattle from 6 to 12 years of age the amount was slightly less, averaging 0.13 mg. per gram for the retina and 1.103 mg. per gram for the adrenals.

In swine from 5 to 10 months old the amount in the retina averaged 0.085 mg. per gram and the amount in the adrenals 0.93 mg. per gram. No constant relation was observed between the amounts present in the retina and adrenals.

GIFFORD, Chicago. [ARCH. OPHTH.]

INFLUENCE OF ULTRAVIOLET RAYS ON THE BLOOD SUGAR CONTENT. E. BENVENUTO, Pediatria **43**:675 (June) 1935.

The influence of ultraviolet irradiations on the blood sugar content was studied in rabbits. Benvenuto found that under normal conditions exposures of short duration (five minutes) produce no modification, but a longer exposure, especially of the ventral surface, brings about a decrease of the sugar content, the extent of which varies from one case to another.

In rabbits which had been given 1 Gm. of a solution of 20 per cent dextrose per kilogram of body weight intravenously, irradiations failed to provoke appreciable modifications.

The author believes that these modifications are under control of the vegetative nervous system.

SIGNORELLI, New Orleans.

ANALYSIS AND SYNTHESIS OF VITAMIN C, THE ANTISCORBUTIC VITAMIN: ITS BIOLOGIC AND PATHOLOGIC SIGNIFICANCE; A CRITICAL REVIEW. AIAZZI-MANCINI, Riv. di clin. pediat. **33**:385 (April) 1935.

This article is a review of the present knowledge of vitamin C, its chemistry and its relation to scurvy and to cellular metabolism.

HIGGINS, Boston.

RESULTS OF AN EXPERIMENT ON THE PROPER FEEDING OF CHILDREN BETWEEN THREE AND SIX YEARS OF AGE. MIGUEL A. JAUREGUY, Bol. Inst. internac. am. de protec. a la infancia **8**:413 (April) 1935.

The author is the physician of a luncheon room for poor children of preschool age. In two years there was an attendance of one hundred and eighty-seven children; only twenty-six of these attended during the two years, and the conclusions drawn refer to them only. It was estimated that they got only one substantial meal a day, since the food eaten in the homes was not taken into account.

The conclusions were as follows:

Proper feeding as to quality and quantity, based on only one daily meal, among twenty-six children aged between 3 and 6 years, resulted in an average increase in weight of 3,500 Gm., that is, 194 Gm. a month during eighteen months. This increase was rapidly noted in the first year of the change in feeding, but it afterwards became much slower.

With this diet the children attained a balanced weight in the first year.

Increased weight is not always a sign of improvement in the general health, and, owing to the opposition of negative factors, it may coincide with a fall of the index strength.

Meals in common for needy children between 3 and 6 years of age are physically and psychologically advantageous.

LESLIE, Evanston, Ill.

AN INTRODUCTION TO THE STUDY OF NUTRITION IN CHILDREN. PEDRO DE ALCANTARA, J. de pediat., Rio de Janeiro **2**:143 (April) 1935.

This article comprises the first three chapters of a book in preparation by the author. The chapters deal with nutrition in general, its importance to the child, an estimation of the state of nutrition and a general view of the causes of poor nutrition.

SANFORD, Chicago.

RÔLE OF CEREAL AND SALT IN EXPERIMENTAL RICKETS. P. GYÖRGY, G. POPOVICIU and TAMOTSU SANO, Ztschr. f. Kinderh. **55**:442 (Sept.) 1933.

According to the authors, the production of experimental rickets in rats depends not only on a deficiency of vitamin D and the calcium-phosphorus quotient in the diet but also on other unspecific factors, such as the nature of the starch and the amount of salt in the diet.

Corn is the strongest rachitogenic factor; then come oats, rice and wheat. The adjustment of the calcium-phosphorus quotient in the various cereals produces no changes. An increase of sodium chloride in the food has an antirachitic effect.

LEVINSON, Chicago.

STUDIES OF RICKETS: I. E. RUSTUNG, Acta pædiat. (supp. 2) **17**:1, 1935.

This is the first of a series of proposed communications by a young Norwegian physician who has been interested in answering some of the following questions: What is the mechanism by which lack of vitamin D affects the metabolism in rickets? Is rickets due to avitaminosis, pure and simple? Why does mother's milk protect an infant more securely against rickets than cow's milk does, although the latter contains more vitamin D? What is the explanation of the occurrence of rickets among fishing folk in those districts where the population consumes cod liver oil in enormous amounts?

Rustung's investigations were conducted in the medical district of Gol, Norway, during 1931 and 1932. The altitude of this section varies from 200 to 1,000 meters above the level of the sea. The mode of living of the inhabitants and the manner in which the population is distributed make the vicinity peculiarly well suited for a study of rickets. Since laboratory facilities were not available, the author employed as diagnostic criteria in determining the presence or absence of rickets only those physical findings which could be appreciated by sight and touch, namely, craniotabes, rachitic rosary and thoracic deformity. These he regards as pathognomonic of rickets. He relegates to a place of secondary diagnostic value cranial bossing, enlargement of the epiphyses of the extremities, marked delay in closure of the anterior fontanel and certain bony deformities; he attributes diagnostic significance to these only when several such stigmas are present in the same person. Obviously, the study relates to well marked or florid rickets.

The following are the most important results of the investigation:

Of 756 school children, 17 per cent gave evidence of having had rickets. Among the children between 3 months and 3 years of age, bony changes indicating active or healed rickets were found in almost 40 per cent; the incidence of rickets was highest in this period. The difference between the morbidity of the two sexes was unimportant. Four infants less than 6 months old were observed who presented debatable evidence of rickets (craniotabes), although their diet was satisfactory; this phenomenon was attributed to deficiencies which had existed in the diet of the mothers during pregnancy. Rustung believes that the high incidence of rickets among the infants whom he studied was due to premature discontinuance of breast feeding or to the exclusive use of a diet of cereal and milk during the last half of the first year of life. The harmful consequences of this one-sided diet were obviated to a certain extent if the infants spent much of their time in the open air.

No relation could be discovered between domiciliary factors and the occurrence of rickets. The homes occupied by the farmers of the region were deficient in sunlight but well ventilated. The atmosphere of the houses was cool and moist in winter. Furthermore, there was no evidence that rickets tended to occur less frequently in summer than in winter; this was surprising "in view of the importance attributed to ultraviolet rays in the prevention and cure of rickets." The disease was less common in infants born in autumn. Dentition and walking were retarded in those infants who had rickets. Among the group of older children the lowest incidence of the disease was found in those who presented the worst physical condition; these were city children who, although they lacked the nutritional and environmental advantages of their country cousins, had been raised by more modern methods.

Appended to the article is a bibliography which refers chiefly to the Scandinavian literature. There are several illustrations. McCUNE, New York.

Hygiene; Growth and Nutrition; Public Health

PROVISIONAL SUMMARY OF MORTALITY STATISTICS FOR THE UNITED STATES, 1932, 1933 AND 1934. Pub. Health Rep. **50**:1442 (Oct. 18) 1935.

There were 1,396,903 deaths from all causes in the United States in 1934, representing a mortality rate of 11 per thousand of estimated population. This is an increase over the mortality rate for 1933, which was 10.7. The rate for 1933 was the lowest reported since the beginning of this collection in 1900. Tables showing the various causes of death are given. SANFORD, Chicago.

PROPHYLACTIC FEATURES OF NURSING HOMES. A. BOHN, Bull. Assoc. internat. de pédiat. prevent. **3**:13, 1935.

The Home for Dependent Babies of the Department of the Seine, of which Bohn gives a somewhat detailed description, differs from similar institutions in that it is intended to prevent the harmful consequences of sending into the country newly weaned babies and putting them suddenly on an artificial diet in the form of boiled cow's milk. The prevention of digestive trouble has been the primary object in view, and this has been attained by careful supervision of the methods of feeding and by progressive adaptation to cow's milk, which is given only after the successive use of mother's milk, buttermilk and condensed milk.

The chief danger of such a babies' home is infection. In this institution the risk is lessened, owing to strict regulations which are strictly enforced, the careful planning of the building, the efficiency of the staff and the elimination of carriers among both the members of the staff and the inmates. All these factors combine to limit the introduction and dissemination of infection.

The babies are taken out into the open air as often as possible, so that when they are sent to the boarding-out centers in the country they are ready to face the change of temperature and climate.

Thus a large number of varied problems of preventive medicine are solved daily in this home. The purpose, excellent equipment and good results deserve the attention of pediatricians. AMESSE, Denver.

PROTECTION OF MOTHER AND CHILD. GEORGES SCHREIBER, Rev. méd.-sociale de l'enf. **3**:1 (Jan.-Feb.) 1935.

Legislative Measures.—The author proposes to the Minister of Public Health the following measures:

1. A speedy vote on the proposed revision of the Roussel law of Dec. 23, 1874, to insure proper medical examination of infants under 2 years placed in nurseries, and to provide also that all children whose parents are beneficaries of aid from any public funds be submitted to regular health examinations.

2. An early vote by the Senate on the proposed law which was adopted by the Chamber on June 28, 1934, dealing with the general organization of hygiene, medical inspection of schools and the protection of public health.

3. Request to the prefects for a stricter application of the law concerned with "assistance to mothers in confinement," of June 17, 1913, by recommending that they establish medical supervision and control of rest, to be vigorously imposed with the assistance of visiting nurses and the centers for maternal and infant protection.

4. A more satisfactory application of the law of "bounty for nursing," of Oct. 24, 1915, by distributing the monthly bounties for six months only but by raising them to 60 francs.

Proposals for Consideration.—1. Creation of a general technical commission for maternal and infant protection, under the Minister of Public Health, similar to the general commission for the prophylaxis of venereal diseases and to the permanent commission for the prevention of tuberculosis and, like them, having for its fulfilment a central technical service; these commissions and the service having for their aim the following program:

(*A*) Services: (1) creation, with the support of the social agencies, of urban and rural centers for maternal and infant protection, considered by the ministerial circular of July 15, 1931, to have oversight of the list of the foster-children and of the children of all ages dependent or receiving aid to any extent, as is done in the departments of the Rhine; (2) creation of departmental and rural maternities, central nursing stations, nurseries with temporary infirmaries, hospitals or pavilions for sick infants and convalescent homes, especially for children under 3 years of age; (3) suppression of pittances as bounties and in their place the grant of the largest amount of material and moral aid to the private agencies already existing which offer guaranties of technical equipment and good management, and (4) application of regulations.

(*B*) Personnel: (1) nomination of departmental technical medical advisors for maternal and infant protection; (2) appointment of physicians having a profound knowledge of child welfare and approved by the regional technical counselor as medical inspectors for the protection of children in the first year, as chiefs of maternal and infant centers and as physicians in charge of foster children and supervised orphanages, day nurseries, etc., and (3) appointment of state social hygiene visiting nurses or midwives with diplomas for training in child welfare for the numerous posts of social assistants, necessary for the functioning of the maternal and infant services.

2. Intervention with the national Minister of Education to see that in all medical schools complete theoretical and practical instruction in child health is made obligatory for all students, through the services of hospitals duly equipped in this respect.

Necessary Resources.—Since it is granted that the *Caisses d'Assurances sociales* have a rôle of prime importance to play in maternal and infant protection and that the law should accord them large powers in this regard, the following measures are recommended:

1. In the provinces in which departmental organizations for maternal and child protection exist offering the intended guaranties of cooperation and technicalities, the *Caisses d'Assurances sociales* and the Red Cross societies should be urged to draw up contracts with them, according to the excellent example of certain departments, e. g., those of the Seine, Seine-et-Oise, Gironde, Meurthe-et-Moselle, Bas-Rhin, Haut-Rhin, and others.

2. In the departments in which these organizations are wanting, the *Caisses d'Assurances sociales* should be asked (in attending to the creation of these agencies) to subsidize the agencies already existing or scheduled, as agreed on by the Minister of Public Health.

SHAW, Evanston, Ill.

Prematurity and Congenital Deformities

TERATOGENIC INFLUENCE OF THREATENED ABORTION. MARIE NAGEOTTE-WILBOUCHEWITCH, Presse méd. **42**:2079 (Dec. 26) 1934.

The author published in 1917 an article entitled "Teratogenic Influence of Attempted Abortion." She believes that the scope of the title should be extended, as there is no difference in the consequences to the child of voluntary attempts at abortion and those of accidental or pathologic threatened abortion. The danger to the child depends on the time at which the disturbance occurs, the nearer the time of conception the more grave the consequences. It is difficult to estimate the percentage of malformations due to this cause, as physicians are likely to concentrate on heredity, syphilis and alcoholism in taking histories and attempts to produce abortion are often concealed by the patient.

Eight cases are reported in which there was a definite history of attempted or threatened abortion, with the following developmental defects in the infants (other suggestive causes in the history having been carefully ruled out): (1) idiocy; (2) epispadias; (3) irreducible flexion of the phalanges and absence of the right radius; (4) multiple deformities, including anomalies in the length of the fingers, supernumerary thumb, harelip, dental erosions, deformity of the maxilla, branchial fibrochondroma, fibrolipoma and angioma; (5) stenosis of the rectum and deviation of the spine, due to the presence of several hemivertebrae; (6) rudimentary glenoid cavity and luxation of the head of the humerus, and (7) lumbar spina bifida and cuneiform vertebrae with gibbous centers.

BIEKER, St. Petersburg, Fla.

AGNESIA OF THE ABDOMINAL WALL IN A NEW-BORN INFANT. G. KOHN, Progrès méd., Aug. 10, 1935, p. 1328.

A boy, born at full term, presented herniation of the right side of the abdomen. The muscles on this side of the abdomen were lacking There was associated bilateral ectopy of the testicles. Roentgenograms showed normal skeletal development. The embryology concerned in the condition is discussed.

LESLIE, Evanston, Ill.

INFLUENCE OF THE DEFECTS AND MALADIES OF THE FATHER ON THE OFFSPRING. H. PAUCOT, Rev. franç. de puériculture **1**:260 (NOV.) 1933.

Consideration of the effect of toxic and infectious factors in the father on the offspring leads to the conclusion that the principles of eugenic prophylaxis should be applied to men as well as to women.

CRANE, Chicago.

MULTIPLE SOMATIC ABNORMALITIES IN A NURSLING. L. NOVOA, An. de Hosp. José y Adela **5**:239, 1934.

A 2 month old girl manifested numerous deformities, including dilatation of the esophagus and stomach, elongation of the colon, femoral hernia on the right side, congenital stridor, torticollis to the right, bilateral syndactyly of the second and third toes, without changes in the bones and darwinian tubercles in the muscle of the left ear. The child's mother had epilepsy. In her family history were several instances of syndactyly and dislocation of the hip joint, while on the father's side were numerous instances of pulmonary tuberculosis and deformity of the spine. The father had adenoids. The father, mother and child belonged to different blood groups. In this case there were grounds in the paratypical as well as in the genotypical lesions for the occurrence of such an abnormal condition. The worst inheritance was the epilepsy of the mother. Eugenic considerations demand measures to insure against further child-bearing or the institution of energetic treatment for epilepsy in case of future pregnancy.

VINTON, New York.

New-Born

DIASTASE CONTENT OF THE BLOOD IN THE FIRST WEEK OF LIFE. VINCENZO MARZETTI, Policlinico (sez. prat.) **42**:1575 (Aug. 12) 1935.

Former studies showed the diastase content of the blood to be increased in pregnancy. In the present study its estimation was undertaken in twenty new-born infants within the first twenty-four hours following birth, at 3 days of age and at 6 days of age. The value for diastase proved to range between 2 and 3 per cent, as against the normal value for adults of 1.5 per cent. The author ascribes the elevation to increased activity not only of the external secretion of the pancreas but also of the internal secretion of this organ. He discusses the possible diabetic effect of the fetus on the mother and of the mother on the fetus.

VINTON, New York.

FAT NECROSIS OF THE NEW-BORN. JOHANNES SCHOEDEL, Monatschr. f. Kinderh. **63**:241, 1935.

Schoedel reports the case of a new-born baby in whom nodules developed on the extensor and exposed surfaces of the skin immediately after birth. These lesions were definitely in the skin and could be moved over the subcutaneous tissue. They were reddish and remained so during the period of observation but were not inflammatory. The diagnosis is that of fat necrosis due to pressure from forceps. The characteristic location and color and the fact that the baby was in excellent condition distinguishes these lesions from scleredema.

GERSTLEY, Chicago.

INTRACRANIAL LESIONS OF THE NEW-BORN DUE TO CHILDBIRTH. HANS HEIDLER, Wien. klin. Wchnschr. **48**: 825 (June 14) 1935.

Heidler describes a case in which death of a new-born infant was attributed to asphyxia. Autopsy, however, resulted in a diagnosis of rupture of the tentorium cerebelli. The lesion produced central irritation of the respiratory center and intra-uterine respiratory movements. The author points out that intracranial lesions during parturition cause death more often than is commonly thought. Intracranial hemorrhages may occur. These may be classified according to localization as follows: subdural, leptomeningeal, intracerebral and intraventricular. The subdural hemorrhages are almost always caused by rupture of the tentorium cerebelli, rarely by a lesion of the veins of the pia mater and even more rarely by rupture of the sinus. Injury to the tentorium is the most frequent traumatic lesion of birth. Leptomeningeal hemorrhages in the form of cone-shaped hematomas in the cerebral and cerebellar hemispheres are usually observed only in premature infants, as are also the ever-fatal ventricular hemorrhages (hematocephaly). In 65 per cent of infants born at term and in 95 per cent of premature infants, intracerebral hemorrhages (often only microscopic) may be demonstrated, usually originating in the vena magna Galeni. This type of bleeding is of more theoretical than practical interest. Of about the same frequency of occurrence are necrobiotic processes in the brain of the new-born. If intra-uterine death occurs at the beginning of labor, special attention should be paid to the possibility of compression of the cervical part of the spinal cord (Föderl). The autopsy should include not only examination of the skull, but also examination of the cervical part of the spinal cord.

ABT, Chicago.

ON THE ELECTROCARDIOGRAM OF NEW-BORN: I. ON THE ELECTROCARDIOGRAM OF THE NORMAL NEW-BORN. HIDEO HORI, MIZUO IMAI and MIKIO SATO, Jap. J. Obst. & Gynec. **18**:325 (Aug.) 1935.

Electrocardiograms were taken for one hundred and twenty-six mature and thirty-four premature new-born infants. All the infants showed a preponderance of the right ventricle. All the waves in all the leads were lower than in older

infants and in adults. Abnormal electrocardiograms were seen occasionally in the case of premature infants for whom they were taken on from the first to the third day.

ADAIR and POTTER, Chicago.

ON THE ELECTROCARDIOGRAM OF NEW-BORN: II. ON THE ELECTROCARDIOGRAM OF ASPHYXIATED NEW-BORN. HIDEO HORI, MIZUO IMAI and MIKIO SATO, Jap. J. Obst. & Gynec. **18**:333 (Aug.) 1935.

Twelve mature and seven premature asphyxiated infants for whom electrocardiograms were made showed a preponderance of the right ventricle and, in a few instances, an inverted T wave or P wave. All the waves were lower than in normal new-born infants. The authors suggest the possible relation between cardiac disease and asphyxia because of the occasional electrocardiographic abnormalities.

ADAIR and POTTER, Chicago.

A STATISTICAL OBSERVATION OF CEPHALHEMATOMA NEONATORUM. M. OSHIMA, Jap. J. Obst. & Gynec. **18**:347 (Aug.) 1935.

Oshima reports one hundred cases of cephalhematoma neonatorum. Seventy-four occurred in infants of primiparous women and twenty-six in infants of multiparous women. Caput succedaneum and peritoneal lacerations were each twice as common in this group as in those cases in which no cephalhematoma occurred.

Pressure on the contact plane of the head is stated to be the main etiologic factor.

ADAIR and POTTER, Chicago.

LIPOGRANULOMA AND ADIPONECROSIS SUBCUTANEA NEONATORUM. G. MOSBERG and E. BEHR, Nederl. tijdschr. v. geneesk. **79**:3050 (June 22) 1935.

Mosberg and Behr observed a case of so-called adiponecrosis subcutanea neonatorum in a boy of 5 weeks. In connection with this case an investigation was made as to the pathogenesis of this disease and its possible connections with so-called lipogranulomatosis. The authors conclude that in the complex of etiologic factors that cause adiponecrosis subcutanea neonatorum an endogenous factor is the prime agent. Trauma has a certain importance as an exogenous cause; in this respect a relationship exists with lipogranulomatosis, in which, however, exogenous factors are predominant. As an important point of difference between these two diseases the chemical process is stressed, which in adiponecrosis subcutanea neonatorum is mainly a deposition of crystallized fats originating from the fatty tissue, whereas in lipogranuloma disintegration of fat occurs. These views could be confirmed experimentally.

VAN CREVELD, Amsterdam, Netherlands.

Acute Contagious Diseases

IMMUNOLOGICAL APPLICATIONS OF PLACENTAL EXTRACTS; EFFECTIVENESS BY ORAL ADMINISTRATION. C. F. MCKHANN, A. A. GREEN, L. E. ECKLES and J. A. V. DAVIES, Ann. Int. Med. **9**:388 (Oct.) 1935.

In addition to summarizing the results obtained in 1,300 children who were given injections of placental extract for the prevention and modification of measles, the authors discuss the effect of the oral administration of the extract. The immunizing properties of placental extract following oral administration was studied by noting the effect on the Dick reaction in patients susceptible to scarlet fever and the effect of the extract in the prevention and modification of measles in nonimmune children who had been intimately exposed to the disease.

A reversal of the Dick reaction occurred without exception within twenty-four hours following the ingestion of suitable amounts of the extract. The negative

state, however, persisted for relatively short periods. The administration of the extract in iced alkaline carbonated water was the most effective means of administration.

Eighty-four patients who were intimately exposed, in their homes, to other members of the family suffering from measles were given placental extract by mouth in doses larger than those used for intramuscular injections.

The results indicate that while the oral administration of the extract was less effective than the administration by intramuscular or subcutaneous injections, further attempts to secure dependable results are justified.

READING, Galveston, Texas.

WHOOPING COUGH. HUGH C. THOMPSON JR., Arch. Pediat. **52**:569 (Aug.) 1935.

An epidemic of twenty-six cases of pertussis occurring in an infants' home is reported. All the patients were less than 2 years old. Every other child was given three doses of pertussis vaccine prepared by the New York State Department of Health, with no apparent effect. Eight patients not receiving vaccine were given elixir of gold tri-bromide. This method of therapy also proved unsatisfactory.

WADDELL JR., University, Va.

PERTUSSIS—ITS BACTERIOLOGICAL DIAGNOSIS. J. J. MILLER JR., California & West. Med. **43**:138 (Aug.) 1935.

Miller points out that since immunization campaigns have been undertaken against diphtheria, pertussis has taken a front rank among epidemic diseases as a cause of death. The most infective period of pertussis is during the catarrhal stage, before the onset of the diagnostic paroxysms. Diagnosis during this stage is made with certainty only by bacteriologic examination. Using a potato-glycerin-blood agar cough plate held 6 inches (15.2 cm.) from the patient's mouth during fifteen seconds of coughing, Miller obtained 78 per cent of positive cultures of Bordet-Gengou bacilli during the first week of the disease. This percentage decreased to 25 during the fifth week of the disease. The author states that the technic is simple and recommends its use as an aid to earlier diagnosis and isolation of infected persons, thereby preventing avoidable dissemination of the disease.

MARSHALL, San Francisco.

A MILKBORNE EPIDEMIC OF BACILLARY DYSENTERY. Health News **12**:161 (Oct. 14) 1935.

Between Aug. 25 and Sept. 15, 1935, in a village of 500 inhabitants, 131 persons had bacillary dysentery. There were no deaths.

Among 42 children a temperature of 103 F. was common. The infection was traced to raw milk from one dairy. One dairyman was found to be a healthy carrier. Few such epidemics have been reported in New York State.

AIKMAN, Rochester, N. Y.

HUMAN VACCINIA ORIGINATING FROM COWPOX. Health News **12**:167 (Oct. 21) 1935.

Cowpox spread through a herd of fifty cows following infection from a milker who had been vaccinated one month before; the site of vaccination had healed in three weeks. One week later, cowpox appeared in cows that he had milked in another herd. Among seven unvaccinated workers on the two farms, typical lesions of vaccinia developed on the hands and forearms of six, and one had lesions on the eyelids and sclera. Lesions developed in one of five workers who had been vaccinated thirty-eight years previously.

AIKMAN, Rochester, N. Y.

DIPHTHERIA OF THE PENIS. M. P. BOROVSKY, J. A. M. A. **104**:1399 (April 20) 1935.

Diphtheria of the penis is rare. In the case here recorded the patient was the youngest one in whom the condition has been reported. In this case an infant of 10 days had diphtheritic inflammation of the penis after circumcision. In five other cases, three authentic and two reported from memory by the Chicago health department, the circumcision was performed by the same mohel. This would point to his responsibility in the development of the disease. In the case reported the infection probably took place during the change of dressings two days later.

BONAR, Salt Lake City.

ECZEMA VACCINATUM: ITS RELATION TO GENERALIZED VACCINIA. F. A. ELLIS, J. A. M. A. **104**:1891 (May 25) 1935.

The vaccine virus is disseminated at times by the blood stream, causing generalized vaccinia. The virus attacks the epidermal tissue specifically, and traumatized areas are more susceptible than other areas. From evidence in the literature and that obtained from a study of the two cases reported in this article it is thought that eczema vaccinatum and generalized vaccinia are essentially the same and that both diseases are disseminated through the blood stream.

BONAR, Salt Lake City.

COLD URTICARIA FOLLOWING MEASLES IN THREE SISTERS. J. L. HOBACKER and H. J. PARKHURST, J. A. M. A. **105**:662 (Aug. 31) 1935.

Urticaria due to cold is not uncommon, but no instance of it following an attack of measles has been reported. Three sisters were affected in such a manner immediately after an attack of measles. The urticarial tendency gradually subsided and disappeared in a year.

BONAR, Salt Lake City.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES. Pub. Health Rep. **50**:765 (June 7) 1935.

For the period of April 21 to May 18, 1935, 705 cases of meningococcic meningitis were reported. This increase was contrary to the usual seasonal expectancy. The increase was in the North Atlantic, North Central and South Atlantic regions. Scarlet fever also showed an increase in Minnesota, North Dakota, Nebraska and Utah. The incidence of poliomyelitis was increased 15 per cent. Measles, influenza, smallpox and typhoid fever showed a decrease. The average death rate from all causes was 12.1 per thousand, which is the highest since 1930.

SANFORD, Chicago.

PROTECTION OF MICE AGAINST MENINGOCOCCUS INFECTION BY POLYVALENT ANTIMENINGOCOCCUS SERUM. SARA E. BRANHAM, Pub. Health Rep. **50**:768 (June 7) 1935.

A fatal septicemia is readily produced in mice by the intraperitoneal injection of sufficient virulent cultures of meningococci. Studies made on these animals with thirty-three polyvalent antimeningococcus serums showed a marked protection by a number of them. Five antitoxins that were included compared well with the usual antibacterial serums in protective action. Normal horse serum also afforded a certain amount of protection, which varied greatly among individual horses. As a rule, the normal serum protected only when it was given undiluted, whereas some of the immune serums gave protection in dilutions of 1:100 or even higher.

SANFORD, Chicago.

SUMMARY OF CURRENT PREVALENCE OF COMMUNICABLE DISEASES. Pub. Health Rep. **50**:891 (July 5) 1935.

For the period of May 19 to June 15, 1935, meningococcic meningitis and scarlet fever showed a decrease in the number of cases. The number of cases of measles also decreased. Poliomyelitis showed an increase, 240 cases having been reported. The average death rate was 11.3 per thousand of population, which is higher than for any year since 1930.

SANFORD, Chicago.

SUMMARY OF CURRENT PREVALENCE OF COMMUNICABLE DISEASES. Pub. Health Rep. **50**:985 (Aug. 2) 1935.

For the period of June 16 to July 13, 1935, the number of reported cases of poliomyelitis rose to six hundred and fifty-three. This high incidence was not general but was confined to a few states—North Carolina, Virginia, Tennessee, California and New York. All other diseases showed a decrease. The weekly death rate was 10.1 per thousand of population, while the average for the last four years was 10.2.

SANFORD, Chicago.

THE CONTROL OF COMMUNICABLE DISEASES: REPORT OF A COMMITTEE OF THE AMERICAN PUBLIC HEALTH ASSOCIATION. Pub. Health Rep. **50**:1017 (Aug. 9) 1935.

This is the revision of the 1926 report on the control of communicable diseases. It follows the method of outline of the former report and contains instructions for dealing with all the contagious diseases.

SANFORD, Chicago.

TRACHEOBRONCHIAL DIPHTHERIA. HOMER DUPUY, South. M. J. **28**:948 (Oct.) 1935.

Dupuy points out that diphtheria implanted in, and limited to, the tracheobronchial tract is a distinct clinical entity and occurs infrequently in practice. The diagnosis of this condition is easily missed.

Striking symptoms are difficult breathing, with distinct stridor over the trachea; croupy cough, and cyanosis. In practically all cases there is suprasternal and diaphragmatic *tirage* (sinking in). There are wheezy, asthmatic pulmonary sounds. The throat is free from diphtheritic membrane. The voice is normal. The latter sign is an extremely important differential point, because in laryngeal diphtheria there is always dysphonia.

The presence of a foreign body must be positively eliminated.

Microscopic examination of the material from the throat is undependable. Low tracheotomy is the method of procedure to be followed in cases of this condition, particularly in children. Suction through a soft rubber catheter introduced through the tracheal tube often successfully removes a large part of the membrane.

SCHLUTZ, Chicago.

THE CONTROL AND PREVENTION OF WHOOPING COUGH. DAVID GREER, Texas State J. Med. **31**:215 (July) 1935.

Greer emphasizes the seriousness of whooping cough, as shown by statistics on the mortality. He urges that more strenuous efforts be made to diagnose the disease early and to isolate the patient from other children. He believes that the use of vaccine will help cut down the number of cases.

MOORE, Dallas, Tex.

SCARLET FEVER: ATTEMPTED IMMUNIZATION IN A PUBLIC SCHOOL. L. R. LEMPRIERE, Brit. M. J. **2**:450 (Sept. 7) 1935.

The record of attempted immunization against scarlet fever during an outbreak in public schools in 1935, together with the bacteriologic findings and the results, is presented.

ROYSTER, University, Va.

CARRIERS AND RETURN CASES IN SCARLET FEVER. W. A. BROWN and V. D. ALLISON, J. Hyg. **35**:283 (May) 1935.

Cultures taken from the nose and throat of 808 patients with scarlet fever just prior to their discharge from the hospital showed a carrier rate of hemolytic streptococci of 82.8 per cent. The organisms were found mainly in the throat (only 33 per cent of the patients had positive nasal cultures). Thirty of the 808 (3.7 per cent) became infecting carriers after discharge and gave rise to 40 (4.9 per cent) return cases. The rate for cases due to infecting carriers depended largely on how heavy an infection the carrier had, which was determined by the percentage of the colonies of hemolytic streptococci growing on the culture plate. The duration of the patients' stay in the hospital beyond the fourth week increased rather than decreased the infectivity rate of the carriers up to the eighth week.

It was concluded, in view of the high carrier rate on discharge, that examinations of swabs from patients with scarlet fever are of no value in the detection of probable infecting carriers.

The causal connection between "infecting cases" and "return cases" is strongly supported by finding the same serologic type of Streptococcus pyogenes in both types of cases. The patients who had complications in the hospital were slightly more liable to become infecting carriers than those in whom the course was uncomplicated. The commonest age group for infecting carriers is from 5 to 10 years. In most (70 per cent) of the return cases the condition occurred within fourteen days.

Overcrowding, on the one hand, and tonsillectomy, on the other, were not important factors. The administration of antitoxin seemed to make the patient less likely to convey the infection on discharge. JANNEY, Wauwatosa, Wis.

ONE HUNDRED AND SIXTY-SIX CASES OF DIPHTHERIA CORRELATED WITH THE TYPES OF BACILLUS DIPHTHERIAE CONCERNED. J. F. MURRAY, J. Path. & Bact. **41**:97, 1935.

One hundred and sixty-six strains of Bacillus diphtheriae were examined as regards their appearance on McLeod's medium, their morphology and their fermentative reactions. It was found possible to classify them into the three types described by McLeod. There were, however, two subgroups in the gravis type, also in the "intermediate" type. It was found that each type had a predominant morphology associated with it. The gravis type was not found to be associated with a severe type of clinical condition. The clinical conditions associated with the "intermediate type were of greater severity than those associated with the mitis type." FROM THE AUTHOR'S SUMMARY. [ARCH. PATH.]

STUDIES OF THE WATER METABOLISM OF INFANTS WITH DYSENTERY. LADISLAUS VON KOSTYÁL, Arch. f. Kinderh. **105**:20, 1935.

Studies of the effect on the infant with dysentery of giving water by mouth, either alone or in combination with sodium chloride or endocrine extracts, yielded unsystematic and paradoxical results. In most cases the reaction is an increase in the loss of water from the body, usually by extrarenal routes, rather than promotion of the retention of water. This reaction is considered to be due to a disturbance of the central regulatory center, as well as to altered tissue reactions.

CRANE, Chicago.

ELECTROCARDIOGRAPHIC STUDIES ON CHILDREN PREVIOUSLY SICK WITH DIPHTHERIA. E. KIELHORN, Monatschr. f. Kinderh. **61**:406, 1935.

Kielhorn examined one hundred and two children aged from 4 to 16 years who had suffered from diphtheritic myocarditis from one to six years previously. In

this group eighteen complained of fatigue, dyspnea, cardiac palpitation and fainting spells, but for only three were there abnormal electrocardiograms.

Twelve of the children showed definite clinical myocarditis, with only seven positive tracings. In twenty there were changes in the electrocardiogram. These consisted mainly of prolongation of the conduction time, extrasystoles, broadening of the initial complexes and duration of the systole and rather small excursions in all leads. There were frequent changes in the P wave, which are not explained.

Sixty-five per cent showed no clinical symptoms. GERSTLEY, Chicago.

PATHOGENESIS OF THE CEREBRAL COMPLICATIONS OF WHOOPING COUGH. CAROLA VOR DEM ESCHE, Monatschr. f. Kinderh. **61**:446, 1935.

The author studied the cerebral manifestations in 1,115 cases of whooping cough that had occurred since 1923. One hundred and seventy-two of the patients, or 14 per cent, showed cerebral complications. The mortality in the uncomplicated cases of pertussis was 12 per cent, while in those in which there were cerebral symptoms it was 60 per cent.

She divides the cases into two groups: those in which there was definite organic injury to the nervous system and those in which the symptoms seemed to be due to the specific toxin of the disease.

Of the 134 cases in the first group, 20 were cases of meningitis; 40 were cases of convulsions associated with pneumonia; 40 were cases in which the symptoms seemed to be on a constitutional basis, such as spasmophilia, and 8 were cases in which the symptoms developed with the onset of other infections. There were small numbers of miscellaneous causes, such as toxic hydrocephalus, hemorrhage, pachymeningitis haemorrhagica interna and embolism. There were 38 cases in the group that were classified as due to the specific pertussis toxin.

The great lesson from this study is that in the course of whooping cough symptoms from the nervous system may be due to a host of different causes and are usually of grave significance. GERSTLEY, Chicago.

CASE OF SPONTANEOUS POLIOMYELITIS IN A CHIMPANZEE. WALTER MÜLLER, Monatschr. f. Kinderh. **63**:134, 1935.

A case, with observations at autopsy, is reported in which poliomyelitis developed spontaneously in a chimpanzee. The animal had been allowed considerable freedom and had unrestricted contact with human beings. For instance, two days before the onset of the paralysis, he had gone to a schoolroom, in which poliomyelitis developed in two children within seven days. GERSTLEY, Chicago.

SCARLET FEVER FOLLOWING TONSILLECTOMY. R. MITTERMAIER, Ztschr. f. Laryng., Rhin., Otol. (Teil 1: Folia oto-laryng.) **26**:134 (June) 1935.

Mittermaier reports that in the years between 1930 and 1934 he observed ten children in whom scarlet fever developed following tonsillectomy. Three of the cases of scarlet fever occurred close together so that a transmission seems possible; three other cases occurred at a time when the disease was rather prevalent, and it is possible that in these cases tonsillectomy was performed during the period of incubation. The other cases, however, occurred at long intervals. The scarlatina always appeared on the second or third day after the tonsillectomy with a sudden febrile temperature and with a more or less pronounced exanthem. The hemogram always disclosed leukocytosis and also eosinophilia. The urobilinogen reaction was positive, as was also the blanching phenomenon. The fever and exanthem disappeared within a few days, and the desquamation took the usual course. There were no complications involving the kidneys or other organs except that in one case there developed swellings and suppurations of the cervical glands, the pus containing hemolytic streptococci. The author evaluates three etiologic theories of scarlatina, namely, the theory that it is caused by a special

pathogenic micro-organism, the theory that hemolytic streptococci cause it, and the opinion that an unknown virus, which supposedly is closely connected with hemolytic streptococci, is the causal factor. In any event, it is likely that chronically infected tonsils are the foci of infection. The author further discusses whether there is a difference between the ordinary epidemic scarlatina and the so-called wound scarlatina. He is convinced that the latter is a true scarlatina, for it presents all the aspects of scarlatina. Then he evaluates the rôle played by the tonsils in the causation and course of scarlatina and reaches the conclusion that it has not been definitely explained as yet. He thinks that postoperative scarlatina might be more frequent than is generally assumed and hopes that his report will induce others to watch the incidence of this form of scarlatina. He suggests that they observe whether the disease always takes a comparatively mild course as in the cases observed by him.

Acute Infectious Diseases

Acute Rheumatic Fever: Its Prevention and Treatment in Childhood. Harry Apfel, Arch. Pediat. **52**:407 (June) 1935.

Nothing new.

Waddell Jr., University, Va.

Welch Bacillus Infections. Treatment by Autofiltrate Method. George R. Dawson Jr., J. South Carolina M. A. **31**:111 (June) 1935.

There are three types of gas bacillus infection. Bacillus Welchii is the cause of the condition in 82 per cent of the cases. The outlook depends on the virulence of the organism, the part affected and the treatment. The review of the cases in the Roper Hospital reveals that 83 per cent of the patients who did not receive filtrate died, while of those who received Welch bacillus filtrate only one died—a mortality of 11 per cent. Amputation is not advised. One case is reported by the author.

Weston Jr., Columbia, S. C.

The Effect of Administration of Vitamin C on the Reticulocytes in Certain Infectious Diseases. James M. Faulkner, New England J. Med. **213**:19 (July 4) 1935.

The effect of the administration of large doses of vitamin C daily has been studied in twenty-seven cases of rheumatic fever, eight cases of tuberculosis of the bone and two cases of Still's disease. In each of the disease groups patients with both active and inactive processes and recovered patients were included. None of the patients showed any clinical signs suggestive of scurvy. All the patients had been on a diet generally considered to be adequate in vitamin C. The thirty-seven patients varied in age from 3 to 25 years, with an average of 10.6 years. All were given additional vitamin C in the form of 530 cc. of orange juice per day by mouth or in the pure crystalline form in daily doses of from 200 to 300 mg. by mouth and, in two cases, intravenously.

No specific therapeutic effect on the course of the disease was observed during the period of the administration of increased amounts of vitamin C, which lasted, on the average, for four weeks.

In the majority of these cases a response of the reticulocytes followed the large doses of vitamin C, analogous to the reaction which follows the administration of vitamin C to patients with the anemia of scurvy. The previous administration of large amounts of iron in the form of ferrous sulfate did not prevent the occurrence of the reticulocyte response.

An interesting feature of the reticulocyte response is the fact that it was roughly proportional to the severity of the infection. The etiology of the infection was not the controlling factor in conditioning the reticulocyte response. The results suggest that in infectious diseases relative vitamin C deficiency commonly develops and may constitute a secondary complication of some importance.

Gengenbach, Denver.

CUTANEOUS REACTIONS TO HEMOLYTIC STREPTOCOCCUS NUCLEOPROTEIN IN RHEUMATIC AND NON-RHEUMATIC CHILDREN. ALBERT D. KAISER and JOHN D. KEITH, New York State J. Med. **35**:69 (Jan. 15) 1935.

Intradermal skin tests were made with a heat-stable extract of hemolytic streptococci. Eight hundred and thirty-five children were tested. Positive skin reactions were rare in infants, but the number increased with age. Of 200 rheumatic children, 75 per cent gave positive reactions. Positive reactions were found in 51 per cent of children who had had tonsillitis. Of children with scarlet fever, 71 per cent gave positive reactions. A positive reaction demonstrates that the child has at some time been infected with hemolytic streptococci. Retesting children after tonsillectomy showed a reduction of positive reactions. The study supports the hypothesis that rheumatism is caused by the streptococcus. It is suggested that the test be performed, together with the tuberculin test, to determine the etiology of erythema nodosum.

In scarlet fever the percentage of positive reactions increases progressively with the course of the disease, reaching a maximum in the fourth week.

AIKMAN, Rochester, N. Y.

TRANSMISSION OF KALA-AZAR IN CHILDREN. E. BENHAMOU, Paris méd. **2**:365 (Nov. 2) 1935.

The principal points brought out in this discussion of kala-azar are as follows: (1) The virus lives in large numbers in the skin of infected human beings and dogs and may be found in scrapings of the skin. (2) The intermediary host is probably the sand-fly, one of the genus Phlebotomus. (3) Prophylaxis consists in early recognition and treatment of infected human beings and dogs and preventing access of the sand-fly to these and also in preventing access of the sand-fly to healthy persons, by adequate screening. The report comes from Algeria.

LESLIE, Evanston, Ill.

PROPHYLAXIS AGAINST ACUTE ARTICULAR RHEUMATISM. DEWET BARBATO, Arch. de pediat. d. Uruguay **6**:462 (Nov.) 1935.

True prophylaxis lies in the proper education of parents in regard to the significance of rheumatic manifestations, even the mild ones, and the dangers to the child if unrestricted activity is permitted and the condition is allowed to go on untreated. The author proposes the creation of special commissions under the direction of public health officials, which would prepare special propaganda and sponsor educational measures to give proper information on this subject to the public.

SCHLUTZ, Chicago.

CLINICAL EXPERIENCE WITH SEROLOGIC REACTIONS IN INFECTIOUS DISEASES. C. VON HEGLER, Deutsche med. Wchnschr. **61**:447 (March 22) 1935.

In typhoid fever agglutination beyond a dilution of 1 : 100 appears after the first week of the disease. With several other infectious diseases there is occasionally mild group agglutination. However, in the course of disease the specific typhoid agglutinins increase, and the group agglutinins decrease. In mixed infections, the Castellani sedimentation test might be used. There are occasional cases of typhoid in which the agglutinins are not increased. Twelve hours after the injection of 2 cc. of a 5 per cent solution of casein intramuscularly, the agglutinin titer of the patient with typhoid can be temporarily increased.

The agglutination test is a valuable aid in the diagnosis of paratyphoid B. In cases of food poisoning by the Gärtner bacillus high specific agglutinins were often found. The same is true in cases of poisoning with Bacillus proteus. In bacillary dysentery the specific agglutinins appear late in the disease, disappear soon and

in children are present in only small quantities. Although specific agglutinins and complements are present in recurrent fever, the direct search for spirochetes in the blood is simpler.

In typhus fever, the study of agglutinins with Rickettsia Prowazeki is still in the experimental stage. However, the high agglutinin titer with Bacillus proteus X19 is pathognomonic for typhus fever. There is also cutaneous sensitivity, which is demonstrable with a germ-free filtrate of Bacillus proteus X19, a helpful aid in making the diagnosis.

For the diagnosis of Malta fever, the specific agglutinin reaction of a dilution of more than 1 : 200 and the intradermal reaction with "Bang-Lysat" can be of help. Both are, however, only inconstantly positive. Group agglutination with typhus fever is commonly observed.

Weil's disease, or infectious icterus, can be diagnosed by the demonstration of Spirochaeta icterohaemorrhagiae in the blood during the first week of the disease. Later the presence of antibodies, agglutinins or complements is of some help. In psittacosis, inoculation of mice with the sputum of the patient is the most reliable method of diagnosis. In glandular fever the Hanganatziu-Deicher reaction is valuable. It consists of the agglutination of inactivated sheep red blood cells by the diluted serum of the patient. The borderline agglutination titer is 1 : 100. The mallein skin test is the most reliable method for diagnosing glanders. The complement-fixation test is less constant. In cysticercus disease, the specific agglutinin test can be of service. In tularemia there is a high agglutination titer from the second week of the disease on. Bacterium melitense and Bacterium abortus are often also agglutinated.

In endocarditis lenta, the addition of a 30 per cent solution of formaldehyde to the serum produces clouding and gel formation. The same reaction occurs in kala-azar, malaria, syphilis, leprosy and also in tuberculosis. The reaction should be read at from twelve to twenty-four hours. Nephrosis, uremia and amyloidosis may also give false positive reactions.

In malaria, the reaction of Henry might help to make the diagnosis. This test consists of the flocculation of the serum when choroid pigment or certain other protein compounds are added to it. The blood has to be taken between attacks.

KERESZTURI, New York.

EARLY DIAGNOSIS OF PNEUMOCOCCIC INFECTIONS. J. MULDER, Nederl. tijdschr. v. geneesk. **79**:4353 (Sept. 14) 1935.

Mulder gives a review of some recent methods of bacteriologic examination for the detection of pneumococci, especially that making possible direct diagnosis by the examination of sputum or pus by the capsule-swelling method (Neufeld) on the addition of the specific antiserum. He stresses the excellent results of direct culture of a thoroughly washed specimen of sputum or particle of pus in serum broth. In clinical-bacteriologic examination the combination of the capsule-swelling test with culture of the material on blood agar and serum broth almost regularly makes possible an early diagnosis. In Mulder's opinion, the routine inoculation of mice for the identification of pneumococci can be dispensed with in the clinic, which will save time and materials.

VAN CREVELD, Amsterdam, Netherlands.

Chronic Infectious Diseases

AN EXPERIMENTAL STUDY OF THE PROBLEM OF THE EXISTENCE OF AN INVISIBLE FORM OF THE SYPHILITIC VIRUS, AND OF SPONTANEOUS SPIROCHETOSIS IN RABBITS. A. BESSEMANS, J. VAN HAELST and H. DE WILDE, Am. J. Syph. & Neurol. **19**:161 (April) 1935.

As the title states, this article is the report of an experimental study and does not lend itself to abstracting. The authors' conclusions are as follows: (1) A technic for counting spirochetes in lymph glands and in syphiloma has

been presented. (2) With this technic the presence of spirochetes in organs heretofore considered free from these organisms can be demonstrated. (3) Nothing points toward the existence of the hypothetic invisible forms of the virus of spontaneous spirochetosis of rabbits. (4) It is probable that the causal agent of both syphilis and spontaneous spirochetosis is the visible form of Spirochaeta pallida and Treponema pallidoides (Treponema cuniculi).

ROYSTER, University, Va.

TUBERCULOSIS AMONG RURAL AND VILLAGE SCHOOL CHILDREN IN BUNCOMBE COUNTY, NORTH CAROLINA. P. P. MCCAIN, C. D. THOMAS and H. L. SUMNER, Am. Rev. Tuberc. **32**:150 (Aug.) 1935.

Buncombe County, in which this study was made, is located in the heart of the Blue Ridge Mountains. Asheville is the county seat. The children studied were of white, native-born American parentage. Eighty-two per cent of 11,542, or 9,482, pupils were given an intracutaneous tuberculin test with 0.1 cc. of a 1:1,000 dilution of old tuberculin. As far as possible, the positive reactors were given a general physical examination, and roentgenograms of the chest were made in the case of 889 children. Lesions were found in 193. Of these, 173 were classified as having the childhood type of lesions, 9 as having the adult or reinfection type, and 11 as having both the childhood type and the adult type. The highest percentage of demonstrable lesions were in the groups of those aged 6, 8, 9, 10 and 12 years. It was noted that the largest percentage of demonstrable lesions was found in those children who reacted most strongly to the tuberculin test.

The treatment recommended for the various groups was as follows: 1. Children with no demonstrable lesions may lead normal lives, but they should have any defects corrected and be given special hygienic and dietetic care. 2. Those with slight or moderate lesions of the childhood type may continue at school, provided they are given reasonable hygienic and dietetic care. They are to avoid overexercise, lie down for an hour each day and be kept under medical supervision. 3. Those with more extensive lesions of the childhood type should be separated from patients with the open type of disease and should be placed in a preventorium unless rigid precautions to prevent infection of other members of the family are feasible. 4. Children with extensive lesions of the childhood type should be placed in a sanatorium or preventorium, or placed on a modified rest cure at home. 5. All children with the lesions of the adult type, except those with definitely inactive lesions, should be kept at rest in bed at home until placed in a sanatorium.

EUGENE SMITH, Ogden, Utah.

THE INCIDENCE OF TUBERCULOUS INFECTION AND DISEASE IN A PRIVATE SCHOOL FOR BOYS. THOMAS M. HORAN, Am. Rev. Tuberc. **32**:166 (Aug.) 1935.

Examination of one hundred and ninety-seven boys (the average age was between 14 and 15 years) was made by roentgen examination and Mantoux test, and in most cases this was repeated at yearly intervals. These boys were relatively segregated and lived in an environment known, as far as possible, to be free from open cases of tuberculosis. Forty-one per cent gave a positive Mantoux reaction, and 11 per cent showed definite signs of the childhood type of tuberculosis. The percentage of positive Mantoux reactions in three successive years was 47, 41 and 33 per cent, respectively, showing a definite progression toward a negative reaction. It was further observed that after about two years, calcium was deposited in an appreciable degree in the tuberculous lymph nodes, and healing progressed, in the absence of further contacts, with a fading of the tuberculin reaction from year to year until in some cases a negative reaction was reached.

EUGENE SMITH, Ogden, Utah.

RELATION OF ALLERGY TO THE ANTIBODY CONTENT IN ANIMALS VACCINATED WITH BCG. B. J. CLAWSON and A. B. BAKER, J. Infect. Dis. **56**:297 (May-June) 1935.

The authors summarize their results and conclude as follows: In the experiments on animals vaccinated with BCG to study the relation of allergy to the concentration of antibodies in the serum, it was found that there was no definite proportionate or necessary relation between the presence of bacterial allergy, as manifested by the intracutaneous reaction to tuberculin, and the concentration of antibodies in the blood, as indicated by the occurrence of agglutinins and complement-fixation antibodies.

TOOMEY, Cleveland.

REMARKS ON HEREDITY IN RELATION TO TUBERCULOSIS. GREGORY KAYNE, Arch. Dis. Childhood **10**:157 (June) 1935.

The transmission of tubercle bacilli from the mother to the fetus occurs not infrequently, as shown in cases of "evident congenital tuberculosis" and by the presence of tubercle bacilli in infants who were separated from their mothers from birth and died of other causes. Infants with inherited tubercle bacilli probably die in the first few days or weeks of life apparently of nontuberculous causes. There is no evidence that heredity plays any rôle in the causation of the high incidence of tuberculous infection in cases of contact at home. Heredity does not appear to be responsible for the occurrence of tuberculosis in the children of tuberculous parents, at any rate in the first few years of life, provided that postnatal contact has been avoided. Inheritance of a diathesis, or "specific predisposition," may determine the occurrence of tuberculous disease and its prognosis, both in children and in adults, once postnatal infection has taken place.

KELLY, Milwaukee.

IS THE DELICATE CHILD MORE LIKELY THAN THE STRONG ONE TO GROW INTO THE ADULT CONSUMPTIVE? ERNEST WARD, Brit. J. Tuberc. **29**:128 (July) 1935.

Ward answers this question in the negative. It is difficult to coordinate physical development and resistance to disease, but evidence accumulates to force the conclusion that in the debilitated child phthisis is just as likely to develop during young adult or adult life as in the robust or normal schoolboy, but no more and no less so.

EUGENE SMITH, Ogden, Utah.

THE BCG VACCINE AND ITS PRACTICAL APPLICATION. K. NEVILLE IRVINE, Brit. J. Tuberc. **29**:152 (July) 1935.

Irvine, during his tenure of a traveling scholarship, visited many BCG laboratories and clinics in Europe and America to review the position impartially and especially to answer the following questions: (1) Is BCG vaccine safe for children? (2) Does it produce any immunity?

He reviews the question of the return of virulence, the disaster at Lübeck, Germany, and other unfavorable evidence and concludes that if the large number of children who have already received the vaccine is taken into consideration, there seems to be little evidence to suggest that the theoretical danger of a living vaccine has any significance in practice.

As to its value and the amount of immunity produced, insuperable difficulties preclude a definite answer. From the evidence now available, however, it may be asserted that the vaccine produces immunity. While it is wise to hold to the gains thus far made in the control of tuberculosis, there appears to be no valid reason that BCG should not be used as an additional factor in the prevention of this disease. A scheme is presented for the clinical use of BCG in England, where at present the vaccine cannot be obtained.

EUGENE SMITH, Ogden, Utah.

TUBERCULIN REACTION OF HONG KONG CHINESE, WITH SPECIAL REFERENCE TO THE USE OF TUBERCULO-PROTEIN. L. J. DAVIS and J. S. GUZDAR, J. Hyg. **35**:300 (May) 1935.

Of Chinese in Peiping between 8 and 20 years of age, 30 per cent gave positive Pirquet reactions. Of Chinese children in Batavia, 40 per cent under 6 years of age gave positive reactions and 80 per cent of those between 10 and 14 years. In Shanghai in mixed age groups 60 per cent gave positive reactions while 94 per cent of persons over 24 years old gave positive reactions.

In the group of persons of various ages 93.1 per cent gave positive reactions to old tuberculin injected intradermally in a dilution of 1:1,000 and 1:10,000 while in the same group 84.9 per cent gave positive reactions to similar dilutions of tuberculoprotein. The reactions to old tuberculin were the more vigorous.

JANNEY, Wauwatosa, Wis.

INTERSTITIAL KERATITIS, BOOMERANG LEGS AND YAWS IN A EUROPEAN BOY FROM THE NEW HEBRIDES, C. J. HACKETT, M. J. Australia **2**:213 (Aug. 17) 1935.

Hackett reports in detail the case of a 14 year old boy who presented the symptoms of interstitial keratitis, saber-shaped tibias and yaws. The family history was carefully scanned for any positive evidences of congenital syphilis, and that factor was practically eliminated.

The author reviews the literature on the occurrence of interstitial keratitis and saber-shaped tibias with yaws. Saber-shaped tibias with yaws is found more frequently than interstitial keratitis and yaws. The concurrent occurrence of syphilis and yaws is rare; in fact, evidence shows that there is a cross-immunity between these two diseases. This condition responded rapidly to treatment with a brand of neoarsphenamine and potassium iodide and to inunctions of mercury. There was a prompt reversal of a 4 plus Wassermann reaction.

The author concludes that the symptoms were the result of yaws, because the history entirely eliminated the possibility of syphilis as an etiologic factor and the response to the treatment was so rapid.

BAER, Pittsburgh. [ARCH. DERMAT. & SYPH.]

ROENTGEN TREATMENT OF TUBERCULOUS MENINGITIS. J. S. WEINER, E. D. DOUBROW, M. G. FINKELSTEIN and A. A. SCHNEIERSON, Arch. de méd. d. enf. **38**:537 (Sept.) 1935.

Any report of successful treatment of tuberculous meningitis is looked on with justifiable skepticism, and instances of recovery are commonly viewed in the light of an uncertain diagnosis.

Of two hundred and fifty instances of alleged cure the reports of which are scattered through the literature, which were carefully reviewed by Cramer, only sixty-four seemed to warrant scientific consideration. Zimbler and Togonnova have demonstrated the presence of Koch's bacillus in the cerebrospinal fluid of infants suffering from various forms of tuberculosis not accompanied by meningeal involvement. Forster has described a miningocerebellar syndrome simulating in many respects the clinical picture of tuberculous meningitis yet with a favorable prognosis.

One may therefore speculate as to whether in so-called cases of recovery the condition is not meningismus with the accidental presence of tubercle bacilli. If it is admitted that the infection is occasionally curable it must not be assumed that the remedies used are responsible for the cure, as recovery may be spontaneous.

Various therapeutic agents have been employed in the treatment of this disorder, chiefly mercurials and iodides. Attempts have been made through frequent spinal punctures to drain the cerebrospinal system, and pneumo-encephalotherapy has been recommended by Scharp, who reported recovery from this procedure in three of twelve cases.

Bokay introduced the novel method of roentgen treatment and claimed five recoveries in a series of seventeen cases. The authors, having found no authentic instances of relief from the usual management in their extensive clinic at Odessa, determined to follow Bokay's suggestions. The total number of patients was twenty-five. These varied in age from 1 to 13 years. Twelve of these were girls, and thirteen were boys. Temporary amelioration was noted in several cases, but all the children succumbed to the disease in about the usual time.

The conclusion reached was that roentgen therapy does not influence in any material manner the progress of tuberculous meningitis.

AMESSE, Denver.

OBSERVATIONS ON CHILDREN WHO INGESTED BCG VACCINE SOON AFTER BIRTH AND WERE INFECTED DURING SUCCEEDING YEARS. M. COFFIN, Bull. Soc. de pédiat. de Paris **32**:541 (Nov.) 1934.

A report is given of a child who had received BCG vaccine shortly after birth and gave a negative reaction to tuberculin until the age of 4½ years. A positive reaction to tuberculin developed, and evidence was shown of a primary tuberculous infection in the lung. A number of children who had been given BCG vaccine in the regular way in the first days of life had been tested with tuberculin every six months and found to give negative reactions for several years; their reactions became positive at the same time that other children in the families who were used as controls and had therefore not been given BCG vaccine gave positive reactions. In a number of instances there were decrease in weight and evidence of primary pulmonary infection in the vaccinated children, which were indistinguishable from similar occurrences in the nonvaccinated children. A long discussion is appended, which on the whole is not favorable to the use of BCG vaccine.

BENJAMIN, Montreal, Canada.

STUDY OF THE SENSITIVENESS OF THE TUBERCULIN TEST IN CHILDREN HAVING CHRONIC PULMONARY TUBERCULOSIS. H. FLOR and MARINET, Compt. rend. Soc. de biol. **115**:277 (Jan. 20) 1934.

Eighty-eight hospitalized children were tested with infinitesimal doses of tuberculin intradermally. Sixty-seven reacted to less than 0.000001 mg.; two, to 0.000000000000001 mg., and twenty-one, to doses greater than 0.000000001 mg. The sensitivity is, therefore, very great.

Fourteen children were tested at intervals during less than a year after admittance to the sanatorium. There was an increase in their sensitivity varying by several tenths of a milligram. One child only showed a decrease, which occurred during an attack of varicella.

The authors demonstrate the marked sensitivity to tuberculin in cases of long-standing pulmonary tuberculosis, and believe that a definite threshold is established for such a high degree of sensitivity.

WAHL, Cleveland.

CHRONIC SUPPURATIVE CERVICAL ADENITIS IN A CHILD IMMUNIZED BY THE ORAL ADMINISTRATION OF CALMETTE VACCINE. MIGUEL A. JAUREGUY, Arch. de pediat. d. Uruguay **6**:96 (March) 1935.

This condition occurred in an infant who had been immunized with the Calmette vaccine administered by the oral route.

During two months after birth the infant was continually exposed to a patient with massive open tuberculosis. Chronic suppurative cervical adenitis developed, and pus was discharged for months. Neither the Koch bacillus nor the BCG organism could be recovered from the purulent discharge, and there was no growth on culture.

SCHLUTZ, Chicago.

PREVENTION OF TUBERCULOSIS IN CHILDHOOD. M. GONZÁLEZ ALVAREZ, Pediatría españ. **24**:323 (Sept.) 1935.

Prevention of tuberculosis in the adult is not possible unless prophylaxis of tuberculosis is carried out in childhood. It is only by persistence in carrying out prophylaxis in the child that the disease will eventually be conquered.

Prophylaxis of the childhood type of tuberculosis must accomplish two objectives: diminish or prevent the possibility of contagion and increase the child's resistance by every possible means.

The child must be separated from the focus of contagion at the earliest possible moment. The author points out the frequency of such contacts in the schools, the teacher often being affected with the disease and conveying it directly to the pupil. This is particularly true in parochial schools in Spain.

All children should at some time in their lives have a tuberculin test. The test should invariaby be applied after the child has passed through an attack of severe influenza, measles or pertussis.

Prophylaxis is particularly difficult in the home, since the diseased member of the household or immediate environment is often not discovered until extensive damage has been done. The economic condition of the parents and their living conditions are important factors.

The open-air camps advocated by Graucher offer the greatest possibilities for prophylaxis.

The prophylaxis of predisposition concerns particularly the child suspected of being tuberculous or the child unmistakably predisposed to it.

Preventoriums and open-air camps are great factors in providing adequate nutrition, rest and fresh air; these will unfailingly benefit the child and raise his resistance. Seroprevention and sero-attenuation of such diseases as measles, pertussis and grip are additional factors.

The author regards vaccination with BCG according to the method of Calmette as one of the most efficacious measures of prevention.

SCHLUTZ, Chicago.

CLINICAL STUDIES OF CHILDHOOD TUBERCULOSIS IN MANCHOUKUO. YOSHIRO YAMAOKA, MORIYA TANAKA and C. W. HSU, J. Orient. Med. **23**:59 (Oct.) 1935.

This first article by the authors on this subject gives statistical information. Curves are presented showing the incidence of tuberculous infection among the Chinese and Japanese child population of Mukden, and a comparative curve shows the incidence in Japan proper. The incidence for the Japanese in Mukden closely paralleled that for the Japanese in Japan, while that for the Chinese was almost twice as great. Studies of death rates from tuberculosis showed that the heaviest toll is in the first two years, and death is usually due to miliary tuberculosis or tuberculous meningitis. This is much the same condition that holds in Tokio and Kyoto.

LESLIE, Evanston, Ill.

TUBERCLE IN HEALTHY SCHOOL CHILDREN. T. OTA, J. Orient. Med. **23**:109 (Dec.) 1935.

As the result of examination by the roentgen rays and Pirquet's test of forty-eight children selected for their apparent health and good physique among the school children of Dairen, 35 per cent were found to be infected by incubated tubercles.

The result was surprising, as the average height, weight and external appearance of the chosen subjects were above normal.

These results indicate the need for careful examination by the roentgen rays and may indicate some connection between the tubercle and children of apparently robust health.

EDITOR'S SUMMARY.

Diseases of Blood, Heart and Blood Vessels, and Spleen

MYELOGENOUS LEUCEMIA. E. L. JENKINSON, Am. J. Roentgenol. **29**:91 (Jan.) 1933.

The author believes that since the function of the spleen in leukosis is to form leukocytes and also to destroy them and since this additional work increases the size of the spleen, destruction of the spleen through irradiation interferes with these functions. The author concludes that myelogenous leukemia is a disease of the blood-forming apparatus of unknown etiology, that the differential blood count is of great value in prognosis and in the selection of patients for irradiation, that irradiation is of great value and usually produces marked improvement in the condition, that irradiation of the chest produces the best results but that it is problematic whether life is prolonged. STULIK, Chicago.

THE ANEMIC STATE. ROY R. KRACKE and HORTENSE ELTON GARVER, Arch. Pediat. **52**:521 (Aug.) 1935.

The purpose in this article is to summarize the current ideas concerning the factors producing anemia and to emphasize their relationship to the origin and treatment of anemia of childhood. The article is to be concluded in the September issue of the *Archives of Pediatrics* and owing to its very nature and length does not lend itself satisfactorily to abstracting. WADDELL JR., University, Va.

A STUDY OF THE RESPONSE OF THE HEART TO PITRESSIN FOLLOWING THE ADMINISTRATION OF THYROID EXTRACT. C. M. GRUBER, V. H. MOON and E. SUFRIN, Endocrinology **19**:447 (July-Aug.) 1935.

It has been shown that the sensitivity of the rabbit to pitressin is enormously enhanced by the previous administration of thyroid extract. To further investigate this phenomenon the authors studied on the electrocardiogram the effect of the intravenous administration of 0.2 cc. of pitressin to rabbits which had received varying doses of thyroid (from 2 to 8 grains [0.13 to 0.5 Gm.] per day) over periods of from sixteen to fifty-one days.

In twelve control animals mild changes were noted on the electrocardiogram during the injection of pitressin. Among fourteen animals which had been treated with thyroid, the injection of pitressin caused three to die from ventricular fibrillation, one to show temporary fibrillation and the others to show pathologic changes in the electrocardiogram far in excess of those shown by controls.

Thyroid extract given by mouth increased the cardiac rate in rabbits from a normal average of 230 to an average of 360 contractions per minute.

Ninety per cent of the hearts of animals fed thyroid extract showed muscular damage when studied histologically. JACOBSEN, Buffalo.

A METHOD OF EVALUATING CARDIAC PAIN IN CHILDREN. H. C. LUETH and D. SUTTON, J. A. M. A. **104**:1806 (May 18) 1935.

Cardiac pain complained of by children is occasionally associated with severe carditis, but more often it is a harmless symptom. Lueth and Sutton used the Libman test to differentiate between the harmless form and that associated with an advancing pathologic process. This consists of first pressing the thumbs against the mastoid bones and then slipping the forefingers forward against the tips of the styloid processes. Normally, pressure over the mastoid elicits no pain, and in most persons pressure on the styloid tips is painless. The authors found that children who experience no pain after a simple pressure test usually do not complain of cardiac pain and that those who complain of cardiac pain and not after the test almost always have demonstrable cardiac disease. Those with severe pain after the test usually complain of cardiac pain and often do not have any

active cardiac lesion. In acute rheumatic infections cardiac pain and palpitation are valuable aids to the diagnosis of carditis and, unless specifically sought, may be overlooked.

BONAR, Salt Lake City.

THE EFFECT OF DIGITALIS ON ACUTE CARDIAC DILATATION PRODUCED BY ANOXEMIA. E. J. VAN LIERE, G. CRISLER and J. E. HALL, J. Pharmacol. & Exper. Therap. **52**:408 (Dec.) 1934.

Dogs were rendered anoxemic by allowing them to breathe nitrogen through a valve which prevented the rebreathing of carbon dioxide; the cardiac areas were measured on roentgenograms. After the intravenous administration of digitalis there was less cardiac dilatation during anoxemia than before.

PILCHER, Cleveland.

CONVALESCENT CARE OF CARDIAC CHILDREN. PHILIP ROSENBLUM, M. Clin. North America **18**:1471 (March) 1935.

Rheumatism is a chronic progressive infection which may remain latent for years. Attacks confer no immunity but rather create liability to further attacks. Years must elapse before the patient can be regarded as free from risk. The convalescent period of heart disease may be divided into three stages. During the first stage active infection is still present, and absolute rest in bed is imperative. Termination of recumbency should not be advised until the temperature remains normal at least two or three weeks. The pulse rate gives the best information of the actual cardiac state. If the rate while the patient is sleeping is about the same as when he is awake (the alert rate), in the absence of fever, activity can generally be presumed. A recrudescence of the infection is often anticipated by a gradual quickening of both the rate while the patient is sleeping and the alert rate. Extension of the physical signs in the heart usually means activity. The white blood cell count is not reliable, since it may change little in cases of a very active lesion. The sedimentation rate of the red blood cells, in the absence of other acute fevers, is of value and should be determined every few days as a check on activity.

The second stage of convalescence is the period during which cardiac balance is regained and compensation is established, principally by means of carefully supervised exercise, first passive and later active. This is also the time for the removal of any focus of infection likely to cause trouble.

The third stage is that during which the cardiac reserve is built up by means of diet, exercise and supervised play. The ideal setup for such care is the camp for patients with cardiac disease. Rosenblum describes in some detail the regimen of the camp with which he is associated.

EUGENE SMITH, Ogden, Utah.

A STUDY OF HEART DISEASE AMONG VETERANS: III. HEREDITARY AND FAMILIAL FACTORS IN THE CAUSATION OF CARDIOVASCULAR DISEASE. PHILIP B. MATZ, New England J. Med. **212**:977 (May 23) 1935.

Eighty-three, or 18.2 per cent, of the group of four hundred and fifty-four patients studied gave a hereditary or familial history of cardiovascular disease. Fifty-seven of these eighty-three patients, or 68.7 per cent, gave a hereditary history; fifteen, or 18.1 per cent, gave a familial history, and eleven, or 13.2 per cent, gave a combined hereditary and familial history.

A study of the hereditary and familial influence on the various etiologic types of heart disease reveals the fact that they were important factors in the rheumatic (27.7 per cent) and arteriosclerotic (22.9 per cent) types of heart disease, as well as in heart disease the sequel of infectious diseases (15.7 per cent). A parental history of cardiovascular disease was the most frequent finding in those patients with a hereditary history of heart disease, while the presence of cardiovascular disease in a brother was the most frequent finding in those patients with a familial history of this condition.

GENGENBACH, Denver.

STUDIES IN THE ANAEMIA OF INFANCY AND EARLY CHILDHOOD: X. THE ANAEMIA OF INFANTILE SCURVY. L. G. PARSONS and W. C. SMALLWOOD, Arch. Dis. Childhood **10**:327 (Aug.) 1935.

Anemia is a characteristic but not invariable symptom of infantile scurvy. The anemia of infantile scurvy is due to deficiency in vitamin C and is cured by its administration in adequate quantities.

Vitamin C probably functions in the body by forming an oxidation-reduction system, taking up oxygen in the tissues and subsequently, by its power of reversible oxidation, functioning as an oxygen-carrier and thereby playing an important part in the processes of tissue respiration and metabolism. It seems probable that, like thyroxine, vitamin C is responsible for cell metabolism and that its action on the cells of the bone marrow is exerted throughout the whole range of maturation from the endothelial cell to the adult erythrocyte and is not restricted to the stage of maturation of the normoblast.

In the author's opinion the anemia associated with scurvy results from general slowing of the whole process of erythropoiesis, which may be so marked as to result in degeneration and aplasia of the marrow. The resulting anemia is, therefore, usually orthochromic and normocytic. In cases of chronic anemia associated with large hemorrhages into the tissues and from mucous membranes, a posthemorrhagic blood picture becomes superimposed, and the anemia may then become hypochromic. It is conceivable that in extreme cases it may even become truly microcytic.

KELLY, Milwaukee.

ESSENTIAL PURPURA HAEMORRHAGICA. BERNARD MYERS, Brit. M. J. **2**:445 (Sept. 7) 1935.

Two cases of this disease are reported in which splenectomy had been performed. Examination after operation of patients of 9 and 10 years, respectively, showed that they were apparently in good health. Three other cases of the author's are reviewed briefly, with tables of statistical data. This is followed by a general discussion of purpura.

ROYSTER, University, Va.

ANEMIA IN CHILDHOOD. I. WOOD, M. J. Australia **2**:211 (Aug. 17) 1935.

The association of anemia with many diseases is emphasized. The etiology of anemia is discussed, and the disease is divided into the deficiency anemias and the inhibitory or destructive group. The deficiency group is described, with special reference to the supply metabolism of iron. In the inhibitory group anemia of the new-born is described, and treatment by blood transfusion is advocated.

GONCE, Madison, Wis.

INFARCTS AND ANEURYSM OF HEART IN AN INFANT OF NINE MONTHS: SPECIMEN. R. W. B. ELLIS, Proc. Roy. Soc. Med. **28**:1333 (Aug.) 1935.

Photographs of the heart, showing infarcts and an aneurysm at the apex, taken from a patient, aged 9 months, who had died of gastro-enteritis, were shown at the meeting of the Royal Society of Medicine, May 24, 1935.

WILLIAMSON, New Orleans.

HEMOLYTIC ICTERUS IN A BOY TEN YEARS OLD. L. BABONNEIX, MAURICE LÉVY and LAURENT GOLÉ, Bull. Soc. de pédiat. de Paris **32**:281 (May) 1934.

Hemolytic icterus had been present in a boy of 10 years for some time but not from birth, so far as could be determined. He was markedly anemic, and the blood showed a high color index. The degree of icterus varied from time to time. There were no signs of hereditary syphilis or tuberculosis. No accurate family history was obtained, so that it was impossible to know whether there was

any familial tendency in this case. Splenectomy was suggested as the treatment which offered most hope for a cure of the condition. The spleen was considerably enlarged, and the liver was slightly increased in size.

BENJAMIN, Montreal, Canada.

LATE RESULTS OF SPLENECTOMY IN A CASE OF PSEUDOLEUKEMIC ANEMIA. L. BABONNEIX and A. MIGET, Bull. Soc. de pédiat. de Paris **32**:287 (May) 1934.

A girl who had been presented three years previously and had had a splenectomy at that time following a diagnosis of pseudoleukemic anemia was again shown to demonstrate that the spleen is not necessary for life, that splenectomy is the heroic remedy for pseudoleukemic anemia and that it takes a long time for the blood picture to become normal following this procedure.

BENJAMIN, Montreal, Canada.

PRIMARY PERICARDITIS WITH EFFUSION WITHOUT ENDOCARDITIS OR ARTICULAR MANIFESTATIONS; CURED BY THE ADMINISTRATION OF SALICYLATES. M. CASSOUTE, PAUL GIRAUD, MONTUS and TISSOT, Bull. Soc. de pédiat. de Paris **32**:425 (July) 1934.

A boy, 14 years old, was admitted to the hospital with pericarditis with effusion and right-sided pleural effusion. He had been ill for two months, and it was suspected that he might be suffering from typhoid fever. Agglutination tests for the typhoid group of organisms gave negative results. Some of the pleural fluid was aspirated, and no tubercle bacilli were found in it. The sputum, which was scanty, did not reveal tubercle bacilli. The boy had no pains in the joints and no signs of endocarditis. He was given a daily intravenous injection of 1 Gm. of sodium salicylate for ten days and 3 Gm. of this drug by mouth daily for another fifteen days. He made a complete recovery; this is cited as a therapeutic test which confirmed the diagnosis of rheumatic pericarditis.

BENJAMIN, Montreal, Canada.

THE KAUFMANN WATER EXPERIMENT AS A CARDIAC FUNCTION TEST IN CHILDHOOD. S. SYMAN, Jahrb. f. Kinderh. **44**:175, 1935.

Kauffmann's idea that elevation of the lower extremities leads to a washing out of the latent edematous fluid is the basis for this test of cardiac function. After the subject has been flat in bed for four hours the lower extremities are elevated, and the average hourly output of urine after elevation is compared with the average hourly output during the four hour period prior to elevation. An increased output following elevation is considered to be a positive reaction. One hundred centimeters of fluid is given hourly, a total of 600 cc. being taken.

Children from 6 to 14 years old were used. Syman found that those in the stage of latent decompensation had an increased diuresis with elevation of the extremities. He could not confirm the reports of others that similar results were found in healthy persons.

LANDAU, Rochester, N. Y.

REVIEW OF VALVULAR CHANGES IN CHILDHOOD FROM A PRACTICAL POINT OF VIEW. J. HERGLOTZ, Orvosi hetil. **79**:743 (July 6) 1935.

Diagnosis of endocarditis which has developed under one's observation is usually easy, especially when it follows acute rheumatic fever or chorea. In other cases, however, the condition develops insidiously, and the valvular changes become evident after weeks and months only. Roentgen examination does not give much information at first or, at the most, show slight dilatation of the left auricle. Slow sedimentation of the red corpuscles may be the only sign of activity of the process. In these instances diagnosis is difficult because of the existence in childhood of functional murmurs appearing during the growth of the young organism.

School children in Budapest suspected of carditis are examined from two to four times a year. From the standpoint of the school physician, children with cardiac lesions should be divided into three groups: (1) Children with organic murmurs; (2) children with functional murmurs, and (3) children in whom the existence of organic murmur is suspected.

The number of organic heart lesions showed a steady increase among children from 4 to 18 years of age (from 0.66 to 4.64 per cent). The percentage of functional murmurs at the age of 4 was 2 per cent, and at the age of 12, 9 per cent, after which the number diminished rapidly to 2 per cent at the age of 18. The number of children of all ages in whom an organic murmur was suspected was between 1 and 2 per cent.

GÖTTCHE, Budapest, Hungary.

REPORT OF A CASE OF PERIARTERITIS NODOSA IN A FIVE YEAR OLD CHILD. A. VON CHWALIBOGOWSKI and F. GOLDSCHLAG, Pedjatrja polska **15**:96, 1935.

The authors report a case of this malady because of its rare occurrence, particularly in children. Two hundred cases in all have been reported. In Poland six cases were reported. The cause of the disease is unknown. Diagnosis is difficult and is usually made on postmortem examination. The prognosis is poor; most patients die. The disease may last from a few days to several years. The most favorable prognosis is in cases in which there are cutaneous manifestations. The authors give an extensive résumé of the disease.

KRUPINSKI, Chicago.

ANEMIA IN A NEW-BORN BABY. E. MANNHEIMER, Nord. med. tidskr. **9**:881 (May 25) 1935.

A boy, born at full term, weighed 3,760 Gm. at birth. He was breast fed. The mother was healthy and showed a negative Wassermann reaction; the father was unknown. Three younger children have not had any blood disease. There was paleness of the skin since birth. The patient was first examined eleven days later. There was no jaundice. Small petechiae were present in the skin; there was no bleeding from the mucous membranes. The liver and spleen were enlarged. The hemoglobin content was 17 per cent. There were 950,000 red cells and 63,800 white cells, with numerous unripe cell forms. Numerous erythroblasts were present (24 per hundred white cells). The thrombocyte content, bleeding time and clotting time were normal. Treatment consisted of intraperitoneal injections of blood in amounts of from 55 to 65 Gm. and the administration of iron and copper. Amelioration of the anemia followed, and the blood picture was normal at the age of 4 months. The etiology is not known.

WALLGREN, Gothenburg, Sweden.

Diseases of the Ear, Nose and Throat

OTORRHEA: ITS TREATMENT AND COMPLICATIONS. ABRAM H. PERSKY, Arch. Pediat. **52**:302 (May) 1935.

This article adds nothing new to the present knowledge of otorrhea.

WADDELL JR., University, Va.

HUMANISTIC LOGOPAEDY APPLIED TO SPASMOPHEMIA. CHARLES H. VOELKER, Arch. Pediat. **52**:342 (May) 1935.

Voelker discusses stuttering and stammering and suggests certain lines of approach for handling these conditions.

WADDELL JR., University, Va.

THE RÔLE OF DISEASES OF THE NASAL ACCESSORY SINUSES IN HEADACHE. JAMES W. BABCOCK, Bull. New York Acad. Med. **11**:481 (Aug.) 1935.

This paper is part of a symposium on headache given before the New York Academy of Medicine. Headache due to disease of the sinuses is usually worse in the middle of the day, becoming less severe in the late afternoon or evening. This is due to spontaneous drainage following the erect position for from eight to ten hours. In severe cases of acute sinusitis this headache may persist (absence of drainage). The pain in the head is independent of the degree of inflammation.

The location of the pain varies with the involvement of the different sinuses. However, Babcock cautions that not all headaches are due to sinusitis, and only on diagnosis of sinus disease by accepted methods is one justified in attributing the pain in the head to involvement of the accessory sinuses. JAHR, Omaha.

THE PEDIATRICIAN LOOKS AT THE TONSIL. R. M. POLLITZER, J. South Carolina M. A. **31**:146 (Aug.) 1935.

First, the anatomic situation of the three groups of lymphatic tissues are described. Then the indications for removing tonsils are briefly summarized: "after repeated attacks of tonsillitis increasing in severity with or without systemic disturbances." The enlargement of the anterior cervical glands accompanying or following these attacks is emphasized. The experience of Kaiser of Rochester, New York, is quoted. This author concluded that the tonsil is a factor in causing rheumatic fever, scarlet fever and chronic heart disease but that tonsillectomy acts unfavorably in preventing bronchitis, pneumonia and sinusitis.

When it has been decided that the tonsils should be removed a thorough physical examination; a complete blood count, including determination of the coagulation time and the bleeding time, and urinalysis, should be carried out.

This paper provoked much discussion, particularly from otolaryngologists.

WESTON JR., Columbia, S. C.

THE TONSILS AND THEIR RÔLE IN FOCAL INFECTIONS. ABRAM H. PERSKY, M. Rec. **141**:432 (May 18) 1935.

There are two types of tonsils: 1. Large tonsils that produce obstructive symptoms. The ensuing effects of this type are always local. 2. Tonsils that are not enlarged. This type is the real source of danger to the patient, for they produce toxic or focal symptoms. Persky discusses the focal manifestations, first considering certain symptoms of diseases and placing them in certain groups such as (1) the rheumatic group, (2) the cardiovascular group, (3) the genito-urinary group and (4) other groups. In conclusion, he states that the tonsils play an extremely important rôle in focal infections; if they are the only focus, cure can be brought about by their removal, if surgical removal is attempted early before permanent changes have occurred in the tissues. He condemns electrocoagulation.

WILLIAMSON, New Orleans.

HEARING RECLAMATION AND PRESERVATION IN THE MODERATELY DEAFENED CHILD. EDMUND PRINCE FOWLER, New York State J. Med. **35**:287 (April 1) 1935.

Many persons with from slight to moderate deafness do not realize the defect, especially if only one ear is subnormal. Hearing defects in school children are best detected by the 4-A audiometer. When deafness is detected careful functional tests and otologic examinations should be made. Fowler reports on a survey of 600,000 school children in New York City. The study was made possible by funds from the Department of Education and the Civil Works Administration. Two hundred and eighty teachers were given special instruction in lip-reading and in the use of audiometers. Cooperation was secured from medical societies, clinics of hospitals and otologists. The chart used for records is very complete. "The

greatest difficulty is to obtain proper advice and treatment for the nonsurgical cases." Much of the routine treatment generally given to these patients may do more harm than good. Prevention should be stressed in every case. Lip-reading is not only an immediate aid but gives insurance in case of increased deafness. These children should be given front seats in school, and teachers should be instructed in using their lips properly in articulation. Clear enunciation and a good view of the teacher's lips is always important. Moderately deafened children should continue their studies in regular classes. The greatest handicap of the deaf child is not being permitted to hear common words and thoughts of others. Apparent stupidity may be due to this cause. Proper guidance will overcome this handicap, especially if individual hearing devices are provided. "A front seat and individual consideration appear to give greater satisfaction than a hearing aid alone." The children with greater loss of hearing require special attention and instruction. Special schools should be provided for the severely deafened. Recurrent infections of the upper respiratory tract should be prevented when and if possible. Conservative otolaryngologic treatment is stressed.

AIKMAN, Rochester, N. Y.

ACUTE TONSILLITIS: AN ACCOUNT OF SOME RECENT STREPTOCOCCAL INFECTIONS. F. E. CAMPS, Brit. M. J. **1**:1061 (May 25) 1935.

In a definite geographic area, more or less circumscribed, an epidemic of tonsillitis occurred which was more severe than usual. Investigation showed that the main etiologic factor was the beta-hemolytic streptococcus—Streptococcus pyogenes. Other types also occurred. A general description of the outbreak and the predominant symptoms in several cases follows.

The appearance of the throat is described carefully, and an outline of special complications is given; these include acute mastoiditis, cellulitis of the neck, acute nephritis, arthritis, fibrositis and headache. The treatment, both general and specific, is outlined. In a certain number of cases, especially in those in which there was associated nephritis, arthritis or cellulitis, serum was used. Camps thinks that the results justified the use of the serum.

The differential diagnosis is then discussed. The summary is as follows:

"Although cases of scarlet fever have occurred locally during the last year, there has also occurred an epidemic, which has been more severe, of streptococcal tonsillitis, due to one or more types of haemolytic streptococci.

"The majority of the cases showing complications have improved with treatment with polyvalent antistreptococcal serum and the other measures described.

"Before concluding, one question appears extremely relevant: Are we any longer entitled to regard scarlet fever as a separate disease to be accepted by the public health authorities as a ground for notification and isolation?"

ROYSTER, University, Va.

PHARYNGEAL PALPATION IN ADENOID INFECTION. LOUIS LEROUX, Bull. Soc. de pédiat. de Paris **32**:628 (Dec.) 1934.

A child 18 months old had infected adenoids and repeated abscesses of the middle ear. During a flare-up of the nasal infection the adenoid tissue was crushed by pressure with the finger introduced into the nasopharynx. The fever continued for a number of days. The ears continued to discharge mucopus, but the nasal discharge ceased. A short time later the mass of adenoids was removed, and the infection of the ear subsided, the drums assuming their normal appearance in a week. Crushing of the adenoid with the finger in cases in which adenoid infection with fever persists for several weeks and otitis media has developed may be followed by improvement, because, it is conjectured, abscesses within the adenoid, too small to be recognized by palpation, are thus ruptured and drained.

BENJAMIN, Montreal, Canada.

Chronic Ethmoiditis in Children. Louis Leroux, J. de méd. de Paris **55**:503 (June 6) 1935.

Leroux points out that the ethmoid cells develop much earlier than the sphenoid cells, the antrums or the frontal bones. Five cases of chronic ethmoiditis in infants and children are reported. The condition is said to be more frequent than is generally recognized and has as yet been insufficiently studied. Clinically, it occurs most frequently in children who have had their adenoids removed and who have repeated colds and stopped-up noses. Rhinoscopy shows degenerative changes of the middle turbinate bone. The condition may be associated with infection of the other sinuses. No adequate method of treating this condition in children has yet been found.

Leslie, Evanston, Ill.

Tracheal Obstruction Following Tracheotomy; Recovery Following Bronchoscopy. Durieu and Leroy, J. de méd. de Paris **55**:575 (June 27) 1935.

A child on whom tracheotomy was performed for diphtheria showed two days following this intervention an acute obstruction of the trachea, which could not be relieved by the usual means. When the child was apparently in the preagonal stage of asphyxia, bronchoscopy was carried out, and a large mass was extracted which consisted of an agglomeration of false membranes and secretions. Recovery followed.

Leslie, Evanston, Ill.

Mastoiditis in the Infectious Diseases of Infants. A. Fulconi, J. de méd. de Paris **55**:755 (Aug. 29) 1935.

This article consists of a collection of a number of varying opinions as to the etiology, course and significance of mastoiditis in infants. In conclusion one can only say that this condition should always be considered in cases of nutritional disturbances and in cases of prolonged or recurrent otitis media. The operation is one not to be undertaken lightly. Simplification of the technic would be of decided benefit.

Leslie, Evanston, Ill.

The Vegetative Nervous System of Children with Adenoids. Rina Simonetti Cuizza, Riv. di clin. pediat. **33**:641 (June) 1935.

The method of di Jeva (abstract, Am. J. Dis. Child. **40**:655 [Sept.] 1930) was used to evaluate the preponderance of parasympathicotonic (vagotonic) or of sympathicotonic reactions in patients. The effects following injections of epinephrine, atropine and pilocarpine on the pulse rate, the respiration rate, the blood pressure, the skin and the eyes were observed in each child. Of twenty-four children with adenoids, aged from 3 to 11 years, ten showed definite vagotonia; five, sympathicotonia, and the remaining 9, dystonia (i. e., neither vagotonia nor sympathicotonia). Cuizza concludes that children with adenoids should be considered as having dystonia, with a tendency to vagotonia.

Higgins, Boston.

Origin and Significance of Fungi in the Crypts of the Tonsils. G. Sponholz, Frankfurt. Ztschr. f. Path. **46**:390, 1934.

The material on which this study is based was derived from 151 tonsils, 94 obtained surgically and 57 at autopsy. In 105 tonsils, fungi were present in surgical and autopsy specimens in about the same ratio. The fungi were found more commonly in hyperplastic tonsils from patients between 20 and 30 years old. Only occasionally may fungi cause suppurative inflammation. However, they may lead to an accumulation of the material secreted by the neighboring salivary glands and possibly cause formation of sialoliths. The classification of the fungi meets with difficulty. They show some of the characteristics of trichomycetes and some of streptotriches.

Saphir, Chicago. [Arch. Path.]

AN UNUSUAL DISEASE SEEN IN CONSULTATION. K. OXENIUS, München. med. Wchnschr. **82**:1240 (Aug. 2) 1935.

Oxenius reports two cases of fever, supposedly due to an obscure cause, which occurred in consultation. The first patient was a boy, 1½ years old, who had had an irregular temperature, ranging from the normal level to 104 F., for two weeks. Every diagnostic test of which the family physician could think had been performed, but all gave negative results. The child was well nourished and not acutely ill, and the only positive findings on examination were enlargement of the posterior cervical lymph nodes, injection of the uvula and fauces and a retropharyngeal drip of thick purulent mucus. A suitable prognosis was given, and after symptomatic treatment the temperature gradually declined to normal.

A similar case in a girl 2½ years old, with fever of longer duration, is also reported. The author stresses that such conditions are not taught or demonstrated to the medical student, and since such patients are not hospitalized the intern does not see them. It is important to be able to differentiate benign infection of prolonged duration and the onset of a serious condition.

BRAHDY, Mount Vernon, N. Y.

TREATMENT OF DISTURBANCES OF SPEECH AND OF THE VOICE. HUGO STERN, Wien. klin. Wchnschr. **48**:560 (May 3) 1935.

Stern discusses the treatment of the following disorders of speech: (1) dysarthria, in which one sound is spoken poorly, one sound is replaced by another or one sound is left out entirely; (2) stuttering; (3) paraphasia praeceps, in which speech is too rapid and whole syllables are often swallowed or confused; (4) late talking, a condition in which intellect and hearing are normal but in which the child does not seem to want to imitate speech, as the motor speech center is not sufficiently excited by the hearing center; (5) nasalized speech; (6) inferior speech, resulting from poor articulation, lack of tempo and melody; (7) hoarseness, which may be organic or functional; (8) paralysis of the recurrent laryngeal nerve; (9) phonasthenia, or tiredness or weakness of the voice.

In regard to stuttering, Stern states that it produces anxiety, and the anxiety in turn makes the stuttering worse. No two cases of stuttering are ever exactly alike. Of utmost importance in treatment are the personality of the physician and the degree of rapport between physician and patient. The treatment must be started early, and there must be systematic exercises, though the patient must never be made too conscious of the fact that he is being treated for stuttering.

ABT, Chicago.

BACTERIOLOGY AND PATHOLOGY OF CHRONIC OTITIS MEDIA. E. WIRTH, Ztschr. f. Hals-, Nasen- u. Ohrenh. **37**:316, 1935.

Bacteriologic examination of the secretions in cases of chronic otitis media disclosed in the mesotympanal as well as in the epitympanal forms types of microorganisms essentially different from those in cases of the acute type. Only in cases of acute relapse of chronic otitis media are those pyogenic cocci (Streptococcus haemolyticus and Pneumococcus) found which are known to cause acute otitis. In chronic mesotympanal otitis media there are chiefly staphylococci (Staphylococcus albus and aureus) and pseudodiphtheria bacilli. In suppurations of the recessus with marginal perforation and in desquamative processes there usually is found a flora of proteus bacilli mixed with staphylococci, anhemolytic diplostreptococci and occasionally also anaerobic organisms. The especially refractory and severe suppurations of the recessus are caused by an infection with proteus bacilli and fusiform rods. The almost regular appearance of proteus bacilli in chronic desquamative processes of the middle ear suggests that they are causal. To be sure, they are frequently absent in cases of dry cholesteatoma. These observations indicate that often the bacteriologic aspects of a process of the middle ear give indications of the type of the severity of the process. However, the

bacteriologic aspects do not always indicate with absolute certainty whether there exists a harmless suppuration of the tubal and tympanic mucous membranes or a process that has a tendency to produce complications in the upper accessory cavities. Wirth further relates the results of bacteriologic and histologic studies of inflammations of the middle ear of the rabbit. The processes had either developed spontaneously or had been produced by artificial infection. He found that in rabbits chronic processes of the middle ear sometimes develop spontaneously, and that the histologic aspects of these processes resemble greatly those of otitis media in man. If the pathogenic organisms of acute otitis media in the human subject (hemolytic streptococci, pneumococci) are introduced into the bulla of the rabbit they produce acute processes of the middle ear. The introduction into the rabbit's bulla of pure cultures of Bacterium lepisepticum produces at first acute processes in the middle ear, but these assume a chronic character in a comparatively short time. The chronic otitis produced in rabbits by artificial infection does not differ in histologic aspects from the spontaneous otitis. Thus it can hardly be doubted that Bact. lepisepticum is the causal organism of chronic otitis of rabbits. The inoculation of the rabbit's bulla with secretions of human chronic otitis produced various results. The infection did not always take. The mixed floras of fetid secretions from human recessus which contained proteus bacilli and anaerobic organisms proved especially malignant in rabbits in that they produced within a few days necrotizing processes in the middle and internal ears. Secretions containing proteus bacilli frequently produced with great rapidity chronic inflammations of the middle ear with cholesteatoma formations and with the histologic aspects that are evident in spontaneous otitis of rabbits and in that induced by Bacterium lepisepticum. Pure cultures of proteus bacilli from the middle ears of human subjects proved to be of different degrees of virulence for the ears of rabbits. The histologic aspects of the artificially produced otitis of rabbits resemble greatly those of human otitides. EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

Diseases of the Lungs, Pleura and Mediastinum

METHOD FOR REMOVAL OF AN OPEN SAFETY-PIN, POINT UP, FROM THE BRONCHUS. C. P. SCHENCK, Arch. Otolaryng. **20**:424 (Sept.) 1934.

A girl, 10 years old, aspirated a ¾ inch (1.91 cm.) open safety-pin. A roentgenogram showed the pin, point up, opposite the fourth dorsal vertebra. An unsuccessful attempt at removal was made with the 7 mm. bronchoscope. Another roentgenogram showed the pin at the seventh dorsal vertebra. In the second attempt at removal a 9 mm. bronchoscope was used, with a rotation forceps locked in the keeper of the pin and the prong astride the pointed shaft near the spring; the shaft of the prong was fixed by a forceps at the mouth of the tube, the point trailing and straightened as the result of traction on the keeper, and the pin was removed. Recovery was uneventful.

It is claimed that the larger tube facilitates easier manipulation and removal.

GREENWOOD, Chicago.

ORGANIC FOREIGN BODIES IN THE BRONCHI: REACTION OF LUNG TISSUE IN RABBITS. H. J. HARA, Arch. Otolaryng. **20**:549 (Oct.) 1934.

This experimental study, on the reaction of the lung tissue of the rabbit to the intratracheal introduction of solid organic foreign bodies by way of the oral cavity, shows that the pathologic changes produced varied with (1) the character of the foreign body, (2) the manner of bronchial obstruction and (3) the duration of retention. Histologic examination showed that the response of the lung tissue was local, exudative and proliferative, extending from the larger bronchi peripherally. Secondary change was localized pneumonitis, never lobar.

The large mononuclear leukocyte was the main proliferative cell. Vascular changes were obliterative endarteritis with subsequent infarction and necrosis. Capillary hemorrhage in the aveolar wall and in the alveoli depended on the degree of insult. Peanuts, bark of the pepper tree and pop-corn were most irritant. The seeds of oranges, grapefruit, lemons, grapes and watermelon were moderately irritating, while the least reactions were that to bark of the eucalyptus tree and that to cantaloup seed.

In summarizing, the author includes the statements that similar changes were noticed in the opposite lung, where no foreign body was present, and that the primary cause of a drowned lung is the too rapid and excessive outpouring of mucus and exudate in association with an absent or decreased cough reflex.

GREENWOOD, Chicago.

THE VALUE OF HYPERPYREXIA IN THE TREATMENT OF BRONCHIAL ASTHMA. KENNETH PHILLIPS and S. SHIKANY, South. M. J. **28**:801 (Sept.) 1935.

The authors have investigated the value of hyperpyrexia in fifty cases of bronchial asthma, some of which occurred in children. Practically all other therapeutic factors were eliminated.

Clinical and laboratory data seemed to indicate lowered general metabolism in asthma. These findings showed improvement following fever treatments. The clinical results indicate that in approximately 80 per cent of the cases in which treatment was given definite benefit resulted. Biochemical and laboratory studies, however, indicate that in over 40 per cent of these instances relief was possibly only temporary. After observation of six months, 32 per cent of the patients seem to have received lasting relief.

SCHLUTZ, Chicago.

LUNG ABSCESSES AND THEIR TREATMENT. A. J. SCOTT PINCHIN and H. V. MORLOCK, Lancet **1**:1369 (June 15) 1935.

The authors report on fifty-five patients with pulmonary abscess, eight of whom were in a condition in which no treatment was of any avail. In forty-five of the remaining forty-seven patients the condition was considered suitable for bronchoscopic treatment. These included children aged 4, 6, 7, 13 and 14 years, respectively; all recovered.

The authors lay down the dictum that "every case of lung abscess should be watched and treated bronchoscopically so that if necessary operation may be undertaken at the optimum period."

LANGMANN, New York.

AUTOHAEMOTHERAPY IN THE TREATMENT OF BRONCHIAL ASTHMA. K. MADDOX and R. BACK, M. J. Australia **1**:277 (March 2) 1935.

Maddox and Back treated forty-three patients (twenty-four of whom were children) who had bronchial asthma with weekly injections of 10 cc. of the patients' own blood for five injections. Observations were made over an average period of six months. The treatment in the twenty-four children was followed in one group of nine by complete freedom from attacks of significance, in a second group of eight by great reduction in the number and severity of the attacks and in a third group of 7 by reduction in the severity but not in the frequency of the attacks. The results in the cases of the adults were not so striking as in those of the children. The beneficial results obtained were directly proportional to the youth of the patient and therefore to the less complicated character of the asthma. The authors believe that the improvement, especially in adults, is short-lived, but that the "breathing spell" provided by the treatment makes it worth while.

GONCE, Madison, Wis.

CHRONIC (NON-TUBERCULOUS) LUNG DISEASE IN CHILDREN. A. G. MAITLAND-JONES, Practitioner **134**:470 (April) 1935.

Maitland-Jones defines chronic pulmonary disease in children as fibrosis of the lung. In the majority of cases bronchiectasis is found to be an outstanding feature. The etiology, clinical features, morbid anatomic features, diagnosis, prognosis and treatment are given careful consideration. The author deplores the fact that not a sufficient number of children with pulmonary fibrosis have been followed through in order to provide required data on the ultimate prognosis.

SAPPINGTON, San Francisco.

ABSCESS OF LUNG. REGINALD C. JEWESBURY, Proc. Roy. Soc. Med. **28**:1065 (June) 1935.

A case of abscess of the lung in a boy of 8 years is reported. The past history, the history of the illness and the results of physical examination, including a blood count, roentgen examination, bronchoscopy and bacteriologic examination of pus taken directly from the abscess cavity, are given in the report. The report is also accompanied by roentgenograms taken before and after the injection of iodized poppy-seed oil 40 per cent.

WILLIAMSON, New Orleans.

MICRONODULAR LESIONS OF THE LUNGS IN INFANTS. L. RIBADEAU-DUMAS and ALBERT NETTER, Arch. de méd. d. enf. **38**:25 (Jan.) 1935.

In its most elementary form, the parenchymal pulmonary lesion is an alveolitis the character of which depends on such factors as the existing state of the bronchi and the vessels, the perifocal flux, the type of bacteria and their toxins. The authors endeavor to demonstrate that the mechanism of infection and the nature of the terrain on which the first infection develops, in the very young subject, permit anatomic differentiation between angio-alveolitis and broncho-alveolitis.

The origin of angio-alveolitis, essentially a septicemia, may be traced to remote infections such as those of the umbilicus, the digestive tract or the upper respiratory region. Alteration in the vessels dominate the picture; thromboses may be found in the arteries, the veins or even in the capillaries; enormous masses of bacteria may be seen in the distended capillaries, with hemorrhages in the alveoli. Following this one may expect a more or less abundant leukocytic exudate.

Broncho-alveolitis begins commonly with the aspiration of nonsterile liquids and may thus be seen in the new-born. Massive aspirations obliterate the large bronchi and create atelectasis, with acute pulmonary edema; smaller ones yield lesions the evolution of which gives a distinctly septic character to the clinical picture. The infecting substances traverse the bronchi and finally reach the alveoli, producing congestion, edema and leukodiapedesis. Dissemination of the infection now becomes easier.

The reports of four cases are recorded to support these contentions.

AMESSE, Denver.

PULMONARY STEATOSIS. ROBERT DEBRÉ, GEORGE SÉE and E. NORMAND, Arch. de méd. d. enf. **38**:389 (July) 1935.

A case of pulmonary steatosis in a girl of 3 years is reported in detail. The initial invasion was diagnosed as Still's disease and appeared at the age of 16 months; about a year later, diffuse and extensive opacities in both pulmonary fields were seen in the roentgenograms, arousing suspicion of tuberculous involvement. However, cutaneous reactions were repeatedly negative. Profound cachexia, complicated with mastoiditis, brought the case to a fatal termination when the patient was 3 years and 10 months old.

The most significant observations at autopsy were the widespread infiltrations of fat throughout both lungs, including the broncho-alveolar system and the pleura. The lipoid substance was distributed throughout the parenchyma in the

form of droplets of various sizes, some no larger than a red corpuscle and others large enough to be detected with unaided vision. The lungs were indurated through a process of chronic sclerosis; the elastic tissue had disappeared, and many areas were represented by bands of dense connective tissue.

In discussing the pathogenesis of this disease, the authors note that Waters, Bayne-Jones and Rowntree reported in 1917 on an experimental study of the resorption of fats introduced directly into the lungs by intratracheal injections. Various other investigators, in France and in America, made contributions in this field of research. Laughleen published the first clinical-pathologic report under the title of fatty pneumonia; in this survey four cases were discussed. Pinkerton added much, in a further report of six cases, to the clarification of the knowledge of this condition, particularly with respect to the differentiation of various forms; he also suggested a method of determining the nature of the fatty substance by examination of the sputum.

The disease is common enough apparently to warrant careful consideration in the differential diagnosis of pulmonary diseases in infancy and childhood, since practically all the forty-two cases described in the literature concerned very young subjects.

AMESSE, Denver.

CASE OF PNEUMONIA OF A CARDIAC LOBE. ROBERT DEBRÉ, MARCEL MIGNON and BERNARD PICHON, Bull. Soc. de pédiat. de Paris **32**:326 (June) 1934.

An infant, 1 year old, presented symptoms and signs of pneumonia. Roentgenographic examination demonstrated a triangular area of increased density at the base of the right lung, which extended from the hilus, with a somewhat concave outer border toward the diaphragm. This was interpreted as consolidation of the cardiac lobe. The infant recovered. As the density cleared, subsequent roentgenograms showed the presence of a supplementary fissure corresponding to the outer border of the pneumonic area, and this was taken as confirmatory evidence of the presence of a cardiac lobe. It is considered probable that the triangular shadow described in cases of bronchiectasis of the right base may be due to involvement of a cardiac lobe.

BENJAMIN, Montreal, Canada.

FOREIGN BODY IN THE LEFT BRONCHUS: COMPLETE ABSENCE OF COUGH FROM THE TIME OF ACCIDENT UNTIL DEATH. PIERRE PAUL LÉVY and JACQUES SOULLARD, Bull. Soc. de pédiat. de Paris **32**:586 (Dec.) 1934.

A boy, 2 years old, was admitted to the hospital with the history of his having "swallowed" a foreign body and having since been in collapse. He recovered from this state soon after his admission. On physical examination there were found dulness and absence of breath sounds on the left side, with the exception of the apex, where breath sounds were audible. There was no stridor. The patient was pale, and the skin was cold and clammy. Roentgenographic examination revealed the presence of atelectasis of the lower lobe of the left lung, and the diagnosis of a nonopaque foreign body in the bronchus of this lobe was made. The child died, and at autopsy a bean was observed to be tightly lodged in the lower branch of the left bronchus. It is significant that the child had no history of cough from the time of aspiration of the bean until he died.

BENJAMIN, Montreal, Canada.

CASE OF APNEA IN AN INFANT. L. RIBADEAU-DUMAS and MME. SPIRE-WEIL, Bull. Soc. de pédiat. de Paris **33**:45 (Jan.) 1935.

A premature infant had periods of apnea, lasting a minute or two. Lumbar puncture yielded bloody fluid. Necropsy confirmed the diagnosis of intracranial hemorrhage. It is pointed out that apnea resulting from immature development of the respiratory center is usually of the Cheyne-Stokes type, while apnea due to intracranial hemorrhage is more irregular.

BENJAMIN, Montreal, Canada.

Bronchography. J. Gosselin, J. de méd. de Paris **55**:826 (Sept. 19) 1935.

A simple method for filling the bronchi with iodized poppy-seed oil is reported. The patient is placed in the sitting position, with the head slightly back and the tongue firmly pulled forward. A local anesthetic is first introduced through a nasal speculum, and after this the iodized poppy-seed oil. Pulling the tongue forward closes the esophagus, and the oil enters the trachea directly. Roentgenograms are taken as usual.

Leslie, Evanston, Ill.

Treatment of Empyema in Children. Teodosio Valledor and Amador Guerra, Bol. Soc. cubana de pediat. **6**:335 (Nov.-Dec.) 1934.

In empyema in which the pneumococcus is the sole infecting micro-organism, repeated thoracentesis, with as complete evacuation of the pus as possible, should always be attempted. This is particularly true for the young infant. If four or five successive punctures do not clear up the condition, open drainage must be resorted to.

In empyema due to mixed infection, open surgical procedure is, in the opinion of the authors, the only choice. The operation should not be undertaken during the acute stage, except in extreme emergency.

The authors advise against the old classic method of pleurotomy and resection of ribs, with open drainage, and state a preference for the more closed method of pleurotomy, with a valvular system of drainage, described by Gregoire. Two typical cases in which this operation was performed and the favorable results obtained with it are reported.

The operation is performed under local anesthesia. Closed drainage of the affected pleura is employed. The operation proper consists in pleurotomy without resection of ribs.

Schlutz, Chicago.

Possible Errors in the Interpretation of Transverse Roentgenograms in the Child. F. Blanco Rodríguez and F. Gómez Pallete, Pediatría españ. **24**:165 (May) 1935.

In order to avoid wrong interpretation of roentgenograms in pathologic conditions, it is necessary to familiarize oneself with conditions in the normal subject.

Illustrative cases are described, showing how change of position, such as elevation of the arms over the head, distorts a normal picture and how frequently normal shadows referable to the descending portion of the aorta, trachea and ribs may be taken for shadows of the hilus.

Schlutz, Chicago.

Spontaneous Pneumothorax. Manuel Suarez, Pediatría españ. **24**:249 (July) 1935.

The condition, occurring in a child 10 years old, resulted from a hydatid cyst of the lung which had ruptured into a bronchus. Considerable hemorrhage had resulted, and the cavity had become infected. The author believes that surgical treatment of the hydatid cyst is preferable to the expectant treatment based on the hope that the cyst will rupture into a bronchus and in this way will be evacuated.

Schlutz, Chicago.

Encysted Empyema in the Child. Roberto Rodriguez, Rev. chilena de pediat. **6**:381 (Aug.) 1935.

Rodriguez reports eight cases of encysted empyema in children. Two of the patients were treated surgically; in three the process ruptured spontaneously into a bronchus and evacuated spontaneously; two were treated by thoracentesis, and one died.

Encysted empyema is clinically easily differentiated from other conditions, but its extent is not always readily determined. Exact localization and deter-

mination of its etiology are essential to successful treatment. The prognosis depends on the general condition of the patient and the type of treatment elected. The author believes that pleurotomy is generally indicated.

SCHLUTZ, Chicago.

HOMOGENEOUS TRIANGULAR SHADOWS IN THE UPPER FIELD OF THE RIGHT LUNG IN NURSLINGS. YAMAOKA, YOSHIRO and TOSHIO NAKAYA, Monatschr. f. Kinderh. **63**:252, 1935.

Two cases are reported, with eight roentgenograms showing shadows in the upper field of the right lung. The lesions were syphilitic. In the second case autopsy showed that the shadow was due to nonsyphilitic pneumonic infiltration of the upper lobe.

GERSTLEY, Chicago.

PNEUMONIC SEQUESTRUMS IN CHILDHOOD. C. BENNHOLDT-THOMSEN, Ztschr. f. Kinderh. **55**:421 (Sept.) 1933.

Bennholdt-Thomsen reports a case of pneumonia in a child 1 year old, followed by pyopneumothorax and a sequestrum of the upper lobe of the right lung; the latter was demonstrated at autopsy.

The author reviews the literature on the subject. He comes to the conclusion that sequestrums due to pneumococcus infection are rare in childhood and that they are produced mechanically as a result of circulatory disturbance in pneumonia with hepatization.

LEVINSON, Chicago.

TREATMENT OF EMPYEMA IN CHILDHOOD. M. TÉRI, Orvosi hetil. **79**:612 (June 1) 1935.

Empyema should be treated with regard to the individual patient, and indications for treatment should be determined by the age of the child and the characteristics of the disease. Lesser surgical procedures, instead of resection of ribs—aspiration, thoracotomy and trocar drainage—should be used only at the beginning of the empyema, because they seldom lead to definite recovery. Resection of ribs is the procedure of choice by means of which serious complications of empyema may be avoided and rapid and definite recovery may be obtained.

GÖTTCHE, Budapest, Hungary.

Diseases of the Gastro-Intestinal Tract, Liver and Peritoneum

ACUTE APPENDICITIS IN CHILDREN. THE CHALLENGE OF ITS CONTINUING HIGH MORTALITY. HENRY W. HUDSON JR., New England J. Med. **212**:670 (April 11) 1935.

In Massachusetts in 1900 appendicitis was listed as the cause of death of 25 children, while in 1930 it was the cause of death of 107 children. As the general death rate in the age group from 1 to 10 years has steadily declined from 1,290 per hundred thousand in 1900 to 242 per hundred thousand in 1933, the death rate from appendicitis has increased from 5.2 to 15 per hundred thousand. In this thirty-four year period the percentage of all deaths due to appendicitis has risen from 0.5 to 5.3.

Hudson gives an analysis of 100 cases of acute appendicitis observed consecutively in which operation was performed, with emphasis on the time of the operation. Only 28 patients entered the hospital within twenty-four hours after the onset of the attack. One patient with hemophilia died of hemorrhage five days after operation. The remaining 27 were discharged well after an average of twelve and one-half days in the hospital. Drainage was instituted in 8, or 28.5 per cent of this group. Seventeen children were admitted from twenty-four to forty-eight hours after the onset of symptoms. Of these, 3 died, making a mortality

rate of 17.6 per cent. The other 14 were discharged well after an average period of hospitalization of fourteen and nine-tenths days. Drainage was employed in 9, or 53 per cent.

The remaining 55 patients did not enter the hospital until they had been ill forty-eight hours or more. Six, or 10.9 per cent, of these died. Forty-nine spent an average of twenty-one and one-tenth days in the hospital. Drainage was considered necessary in 48, or 87 per cent of this group.

In the community served by the Boston Children's Hospital, early diagnosis and prompt operation constitute the exception and not the rule. Early diagnosis is possible only when parents appreciate the frequency of appendicitis in childhood and when physicians regard the triad of abdominal pain, vomiting and fever in childhood as strongly indicative of appendicitis. Cathartics are contraindicated in the presence of these signs.

GENGENBACH, Denver.

QUESTION OF DEATH FROM EATING A CONFECTION PASSED OUT GRATIS IN A PUBLIC PLACE. WALTER W. FULLERTON, New England J. Med. **212**:975 (May 23) 1935.

A boy, aged 16 years, whose life had been insured with double indemnity in case of accidental death, ate samples of chocolate candy laxative containing a total of about 60 grains (3.9 Gm.) of phenolphthalein. Diarrhea, common nausea and vomiting ensued, and death occurred a week later. At autopsy the pathologic observations included acute fibrinous pericarditis, abscess of the lungs, bronchopneumonia, acute pleuritis, chronic and subacute endocarditis of the mitral valve and a circumscribed abscess of the liver. No pathologic changes were noted that could be attributed to the laxative compound that the patient was said to have eaten. The gastro-intestinal tract was apparently perfectly normal.

GENGENBACH, Denver.

RAW APPLE DIET IN THE TREATMENT OF DIARRHEA. SIDNEY R. KALISKI, Texas State J. Med. **31**:191 (July) 1935.

Kaliski reports satisfactory results in the treatment of twenty-seven children with diarrhea of various types with raw apple. He gives from 10 to 30 tablespoonfuls of scraped apple per day for two days and usually switches to a low residue diet of bland cereal, toast, gelatin, scraped beef and broth. The stools usually become more solid and less frequent within thirty hours, no matter how long the diarrhea had existed before the treatment was begun. In the case in which the diarrhea had the longest duration the condition responded within sixty hours. The author mentions the theories brought forth to explain the efficacy of the diet.

MOORE, Dallas, Texas.

INTESTINAL PARASITES. F. M. B. ALLEN, Practitioner **134**:502 (April) 1935.

Parasites in the intestines of children may, as Allen points out, be the cause of a group of general symptoms. These are mainly symptoms of physical and nervous irritation, but some may be due to toxic conditions produced by the parasites. The intestinal parasites commonly found in England are: (1) threadworms (Oxyuris vermicularis); (2) round-worms (Ascaris lumbricoides); (3) tapeworms (Taenia mediocanellata, Taenia solium and, less commonly, Taenia cucumerina and Taenia nana; (4) flagellate worms (Lamblia intestinalis) now suspected of being a possible cause of certain obscure types of diarrhea, and (5) whipworms (Trichocephalus dispar).

These are discussed individually and in detail, and due consideration is given to the symptoms, diagnosis, treatment and prognosis.

Allen stresses the point that final eradication of intestinal parasites may depend on a restoration of general good health, as a healthy bowel is not a suitable habitation for parasites.

SAPPINGTON, San Francisco.

CLINICAL COURSE AND TREATMENT OF CHOLERIFORM GASTRO-ENTERITIS IN THE INFANT. C. COCCHI, Riv. di clin. pediat. **33**:1104 (Oct.) 1935.

Cocchi presents his analysis of the clinical course and the proper treatment of cholera infantum. By cholera infantum he means an infectious enteritis which is distinctly different from the parenteral diarrhea associated with otitis media, bronchopneumonia and sepsis.

The author recognizes six stages in the course of the disease: 1. The stage of well-being, i. e., that preceding sickness. 2. The stage of alarm. This may last for several hours or as long as eight days. The child appears sick but shows no striking loss in weight. Considerable emphasis is placed on the presence of a deep fissure in the lower eyelid. 3. The stage of toxicity. This lasts from twenty-four to forty-eight hours. The child tends to lose weight rapidly, perhaps as much as from 6 to 8 ounces (170.09 to 226.8 Gm.) a day, and restlessness, stupor, dyspnea, vomiting, fever and secondary infections may be evident. 4. The stage of equilibrium. This lasts from five to eight days. The child shows clinical improvement but does not gain in weight. 5. The stage of recovery. This lasts from ten to fifteen days. The child has an appetite and regains the weight lost previously in the disease. 6. The critical phase. The trend of the child's illness is decided as to whether he continues to do well or whether a chronic nutritional condition develops. Cocchi feels that it is important to establish what phase or stage of the disease the child is in, both in evaluating the seriousness of the condition and in prescribing treatment.

In the treatment of cholera infantum the author especially stresses the value of a cool, humid environment. The temperature of the room should be not higher than 79 F.; this is accomplished by blowing air from a fan across cakes of ice. The children studied were found to do much better clinically in an atmosphere of high humidity than in one of low humidity, for in a dry air children suffer much more than adults from loss of fluid. Starvation is recommended but not for too long a period, that is, not for more than thirty-six hours. In the period of starvation the author urges the administration of sufficient fluid, which may be given as one of the following formulas: (*a*) tea, 2 cc.; water, 1,000 cc.; sugar, 10 Gm., and (*b*) rice flour, 25 Gm.; water, 1,000 cc.; sugar, 10 Gm. When milk feeding is to be resumed, breast milk is preferred, although during the stage of recovery cow's milk is used. During the course of the disease from 140 to 150 Gm. of fluid per kilogram of body weight per day is recommended. Weighing the child every twelve hours is also recommended; thus, one may learn when the child passes from the stage of alarm to the toxic stage. During the phase of equilibrium one must not increase the amount of food too rapidly or a relapse may occur. However, increasing the amount of food too slowly is also bad, as the child may lose appetite and tolerance of food. Cocchi warns against the use of vegetable broths, as these may contain much sodium chloride and are likely to lead to edema. The critical phase occurs when the original weight is regained. At that time one is likely to find the curve for weight showing an up and down fluctuation. This is interpreted as due to protein or nitrogen hunger and warrants the giving of more protein (i. e., cow's milk instead of human milk). When the stools have an alkaline reaction, caution should be exercised against overfeeding, as the child is much more likely to do badly than when the stools are acid.

HIGGINS, Boston.

A CASE OF HEERFORDT'S DISEASE. MARTIN HAFERKORN, Monatschr. f. Kinderh. **63**:161, 1935.

In a 13 year old boy the following developed in rapid sequence: paralysis showing involvement of all three branches of the facial nerves, swelling of the parotid and iridocyclitis. Roentgen examination of the chest showed hilar tuberculosis. There was also a calcified tuberculous focus in the abdomen. The patient also suffered from polydipsia and polyuria, which were, however, not due to dia-

betes insipidus. The latter was ruled out by the ineffectivenss of solution of posterior pituitary. The swelling of the parotid was successfully treated with the roentgen rays. On the basis of these findings the disease was diagnosed as subchronic uveoparotid fever of Heerfordt.

GERSTLEY, Chicago.

ABORTIVE FORMS OF PNEUMOCOCCIC PERITONITIS. J. KRAMÁR, Monatschr. f. Kinderh. **61**:370, 1935.

Kramár reports two cases of beginning peritonitis in which a puncture showed exudate and pneumococci. In both recovery was spontaneous. They are presented as evidence of the existence of abortive forms of the disease.

GERSTLEY, Chicago.

CHRONIC VOLVULUS. SIEGFRIED LIEBE, Monatschr. f. Kinderh. **61**:436, 1935.

In two boys, aged 7 and 8 years of age, symptoms of volvulus developed five months and two and three quarters years, respectively, before death. In each case the symptoms were repeated attacks of abdominal pain and severe vomiting, with prolonged intervals of perfect health.

GERSTLEY, Chicago.

TREATMENT OF PYLORIC STENOSIS IN NURSLINGS. EDMUND NOBEL, Wien. klin. Wchnschr. **48**:306 (March 8) 1935.

The treatment of pyloric stenosis, according to Nobel, may be dietetic, medicinal or operative. If dietetic treatment is undertaken the following rules must be observed:

1. Frequent small meals should be given. 2. Nutrition should be concentrated. 3. The food should be of porridge-like consistency rather than liquid. Nobel is not convinced about the results of medicinal treatment. He has not seen markedly clear results with either atropine or papaverine. As for the operative treatment, most authors are convinced that Rammstedt's operation is the best. For the experienced surgeon it is easy to carry out and gives excellent results. Of the author's thirty-five patients with pyloric stenosis, sixteen were treated conservatively, and nineteen were operated on. The following operations were performed: four gastro-enterostomies (one patient recovered, and three died); three Weber-Rammstedt operations with gastro-enterostomy (one patient recovered, and two died); twelve Weber-Rammstedt operations (six patients recovered, and six died). Nobel discusses the technic of the Weber-Rammstedt operation and the postoperative treatment.

ABT, Chicago.

Nervous Diseases

ARTERIAL CHANGES IN THE BRAIN IN CHILDHOOD. N. W. WINKELMAN and JOHN L. ECKEL, Am. J. Syph. & Neurol. **19**:223 (April) 1935.

The literature is reviewed; etiologic factors are considered, and pathologic changes are described in detail. A detailed description of a clinical case follows, and the authors give the following summary: Eight cases have been reported, of conditions in which cerebral vascular changes simulating arteriosclerosis have been observed in children.

While well developed arteriosclerosis has been described in those cases in which the outcome was fatal, the conclusion is warranted that in cases of infection and toxemia similar, less marked changes occur, which may be the starting-point for the further development of pathologic conditions of the vessels. A clinical case is described to illustrate the gross damage to the brain that can result during a mild infection of the upper respiratory tract, with convulsive seizures. Encephalographic studies revealed softening in the calcarine area to account for the contralateral hemianopia. The prevention of acute infectious diseases of childhood will probably help to prevent many pathologic vascular conditions.

ROYSTER, University, Va.

CEREBRAL BIRTH CONDITIONS, WITH SPECIAL REFERENCE TO MYELOGENY. CLARENCE A. PATTEN and ROBERT A. MATTHEWS, Arch. Neurol. & Psychiat. **34**:61 (July) 1935.

Three hundred and fifty feebleminded patients, having an intelligence quotient of below 50, were studied. About one half of the patients showed definite neurologic signs, but in only 4 per cent of the cases were the signs considered to be postnatal. The authors believed that injury at birth cannot be considered to be the cause of the neurologic condition in an appreciable number of cases. The fact that mental deficiency occurs with and without neurologic complications is presumptive evidence that it is due to structural defects related to failure of evolution in intra-uterine life. Syphilis cannot be held to play a large rôle. The incidence of mongolism increases with the age of the mother. BEVERLY, Chicago.

EFFECT OF INTRACRANIAL TUMORS ON THE SELLA TURCICA. KARL KORNBLUM and LESLIE H. OSMOND, Arch. Neurol. & Psychiat. **34**:111 (July) 1935.

This paper stresses the effect of the various types of intracranial tumor on deformity of the sella turcica. Of 446 cases of verified tumor of the brain the condition caused the deformity in 64.6 per cent. In half of these cases the sella turcica was changed in such a way that the nature of the deformity suggested the location of the tumor. Tumor of the pituitary gland, suprasellar tumor (with or without calcification) and tumor of the temporal and parietal lobes produce the most characteristic changes in the sella and are readily discernible by means of roentgenograms. BEVERLY, Chicago.

ACUTE EPIDURAL SPINAL ABSCESS—A CLINICAL ENTITY. BENJAMIN M. GASUL and RICHARD H. JAFFÉ, Arch. Pediat. **52**:361 (June) 1935.

Three cases of acute epidural spinal abscess in children are reported. The literature on this condition is thoroughly reviewed, and the authors find the reports of sixty-seven cases. These are summarized briefly. The diagnosis seems to depend on the following points: (1) history of trauma, furunculosis or some other infectious process; (2) acute severe pain in the back, radiating along the nerve roots; (3) localized tenderness of the vertebrae in the affected area; (4) clear or xanthochromic spinal fluid, which shows an increase in the protein content and the Queckenstedt sign, and, in cases in which the epidural abscess is located in the lumbar region, thick, purulent material obtained with the lumbar puncture and clear fluid with the cisternal puncture, and (5) paralysis, with incontinence or retention of urine or feces, which comes on within a short period after the onset of the pain. Complete anesthesia below the affected segment, with loss of all reflexes, appears soon afterward.

The treatment consists of early laminectomy and drainage of the area of abscess. The authors believe that laminectomy should be performed even if the culture of the blood is positive and the fluid obtained through the cisternal or lumbar puncture shows an increase in the number of cells and beginning leptomeningitis.

This condition is discussed thoroughly in regard to etiology, pathologic characteristics, diagnosis and treatment. WADDELL JR., University, Va.

ENCEPHALOGRAPHY IN CHILDREN. F. G. LINDEMULDER, California & West. Med. **42**:429 (June) 1935.

Lindemulder presents the diagnostic and the prognostic value of encephalography in children. It is contraindicated in cases of tumor of the posterior fossa and in the presence of infection, either of the blood stream or of a focus near the cranial cavity. In the absence of these two conditions, the procedure is comparatively harmless. The author commonly employs an inhalation anesthesia during the injection of air to obviate accidents from struggling. The air is introduced as the

spinal fluid is withdrawn, each 5 cc. of fluid removed being replaced with an equal amount of air. Ordinarily, 150 cc. of air is sufficient for accurate diagnosis, and in some cases as little as 60 cc. proved adequate. Cases are reported in which adhesive arachnoiditis, external hydrocephalus and diffuse subarachnoid hemorrhage were present.

MARSHALL, San Francisco.

FACIAL HEMIATROPHY ASSOCIATED WITH EPILEPSY: REPORT OF A CASE. DOROTHY E. DONLEY, J. Nerv. & Ment. Dis. **82**:33 (July) 1935.

A white woman, aged 18 years, was admitted to the hospital with complaints of epilepsy and tantrums of jealousy and temper. The first attack of epilepsy occurred at 10 years of age. After the first convulsion, with loss of consciousness, the face was drawn to the left. This facial asymmetry became permanent. Physical examination revealed an underdeveloped woman, 5 feet and 8 inches (172.7 cm.) tall, weighing 113 pounds (51.3 Kg.). There was right hemiatrophy, including the right auricular cartilage, which resulted in elevation of the left eyebrow, deviation of the nose to the right and protrusion of the maxilla and teeth on the left side. Roentgenograms showed atrophy of the bones of the right side of the face, but the vault was not affected. No sensory disturbances were demonstrated. The mental age was 9 years and 3 months. All the laboratory data were within normal limits.

Four convulsions were studied, all of which were similar in the sequence of events. They may be described as follows: The patient noted an unlocalized "snapping" in her head several minutes before the attack; so she had time to remove her glasses, summon a nurse and go to bed before the convulsion. There was sensation of heat in the left subcostal region. Extensor spasm of the extremities was followed by rapid winking of the left eyelid and rhythmic twitching of the mouth to the left, with subsequent conjugate deviation of the head and eyes to the left. The focal twitching quickly gave way to increasing rigidity; the deviation of the head and eyes returned to the midline, and the pupils were dilated and fixed. Bilateral vasomotor changes were equal both in distribution and in intensity. The patient was inaccessible and confused during, and for one hour following, the attack.

The family and the developmental history of the girl is such as to justify the term epileptic personality, with defects in integration running through the entire psychobiologic unit, though the outstanding manifestations refer mainly to pathologic lesions in the diencephalon.

JAHR, Omaha.

THE DIAGNOSIS AND TREATMENT OF CONVULSIONS IN CHILDREN. D. STEWART POLK, M. Clin. North America **19**:247 (July) 1935.

While the differential diagnosis of convulsions in children theoretically requires the consideration of at least half a hundred etiologic possibilities, the problem may be simplified if the factors most likely to be active at different ages are kept in mind. From earliest infancy to 1 month of age the chief causes of convulsions are: cerebral injuries at birth, congenital malformations of the brain and acute infections. From 1 to 4 months of age the toxemia and pyrexia of acute infections of the various systems are chiefly responsible for the convulsive seizures. However, the convulsions may be due to gradually increasing intracranial pressure as a result of cerebral injuries at birth or congenital defects. During the period from 4 months to 2 years of age spasmophilia or infantile tetany, obvious or otherwise, underlies the seizures in a large proportion of cases. Between the ages of 2 and 6 years, poisoning from convulsant drugs, such as strychnine, and chronic lead poisoning are frequently encountered. At this period also acute nephritis in association with uremic poisoning is most likely to occur as a sequel to the acute infections. After the sixth year idiopathic epilepsy leads all other conditions as the most important cause of convulsive seizures in children. For these convul-

sions arising from various causes, the author outlines the usual symptomatic treatment, but especially he urges a careful analysis of causes and the institution of rational therapeutic measures directed to their removal, when possible.

EUGENE SMITH, Ogden, Utah.

THE SIGNIFICANCE OF NERVOUSNESS IN CHILDHOOD. G. W. DISHONG, Nebraska M. J. **20**:7 (Jan.) 1935.

Many factors are involved, including heredity, physical condition and handling in babyhood. Children showing symptoms of malbehavior should have corrective guidance before actual distortion of personality occurs. The mental attitude acquired in childhood may be responsible for later and more serious maladjustments. Many persons are born with an unstable nervous organization, which renders them hypersensitive and susceptible to nervous disorders. A disorderly emotional life may be modified or prevented if recognized in childhood. Children who have fears, who are oversensitive and emotional and who are inclined to tantrums or outbursts of temper are entitled to corrective guidance in order that more serious later developments may be prevented.

HAMILTON, Omaha.

MENINGOCELE, DISPUTED FORM OF SPINA BIFIDA. JACQUES LEVEUF, Bull. Soc. de pédiat. de Paris **32**:328 (June) 1934.

Eight cases of meningocele are reviewed. Meningocele is defined as a simple diverticulum of the subarachnoid space free from any cord elements. The chief danger of the abnormality is possible rupture of the sac and the development of meningitis. In cases in which the overlying skin is thick this danger hardly exists. Most patients with simple meningocele present no other congenital abnormalities.

Operation was performed on these patients, one of whom was a girl 19 years old, with good results, except in one case in which the patient was operated on by another surgeon and died. The menace of the development of postoperative hydrocephalus in cases of simple meningocele is considered to be a myth. The patients were examined years later by a neurologist, and a few showed minor neurologic findings which would indicate some involvement of nerve fibers. They developed well mentally and physically. Histologic examination of the wall of the meningocele showed some aberrant islets of neuroglia in some cases. It is believed that bits of ectoderm, from which the neuroglia develops, were tucked away in the wall of the meningocele during the formation of the spinal cord.

BENJAMIN, Montreal, Canada.

Psychology and Psychiatry

CHRONIC POST-ENCEPHALITIS IN JUVENILE DELINQUENTS. MATTHEW MOLITCH, Am. J. Psychiat. **91**:843 (Jan.) 1935.

Postencephalitic manifestations are often not recognized because of the difficulty of obtaining a history of the acute stage of the disease. Symptoms of chronic postencephalitis are usually slow in their onset, and months or years may elapse before definite signs may be elicited. Some of the criteria for aid in diagnosis are paralysis of convergence, strabismus, visual deficiency and fine intention tremor of the closed eyelids, outstretched fingers and the tongue. Ornsteen's triad (posture of the fingers in repose, spacing of the fingers of the outstretched hand and limitation of motion in the thumb-forefinger test) illustrates the poverty of motion associated with postencephalitis. Lagging of an extremity in walking may be the earliest suggestion of the onset of parkinsonism. Hypersomnia and rapidly developing obesity often exist. Excessive salivation and sweating are rarely seen in early cases. Fixity of expression is also a later symptom.

Of special interest in this syndrome is the changed behavior pattern, which may occur within a few days after the onset of the acute attack or weeks, months or years later. The entire personality of the child may be altered, and the variety of new behavior traits may be unlimited, ranging from mild deviation from normal

conduct to the most serious asocial criminal behavior. The mental state seems to suffer from "a loss of inhibitions over the primary emotions."

The mentality of these children is usually impaired by the disease, deterioration being greater the younger the child at the time of onset of the acute stage.

Treatment is entirely symptomatic. JAHR, Omaha.

TREATMENT OF PROBLEM CHILDREN IN A PSYCHIATRIC HOSPITAL. HOWARD W. POTTER, Am. J. Psychiat. **91**:869 (Jan.) 1935.

Hospitalization of problem children may be resorted to when treatment cannot be carried on at home or when brief periods of institutional care may be necessary for complete diagnostic service. Psychiatric hospitals may be of value in the treatment of the following types of maladjusted children: (1) children whose conduct is such as to require a controlled environment (postencephalitic and psychopathic patients), (2) children with neuroses and psychoses, who need more systematic psychotherapy than the outpatient clinic affords, (3) children whose home environment is such as to make adjustment impossible and (4) children who need the care of a foster-home but whose conduct is such that special types of homes must be selected. Diagnostic service with brief periods of hospitalization are desirable in the group in which (1) asocial behavior is suspected to have an organic basis, (2) functional behavior problems require further psychometric study and (3) combined organic and functional disorders may exist and it is necessary to establish the rôle of each of these factors in the manifestations of behavior.

Admission, procedure, personnel and treatment are discussed.

JAHR, Omaha.

POST-ENCEPHALITIC BEHAVIOR DISORDERS: A TEN YEAR REVIEW OF THE FRANKLIN SCHOOL. EARL D. BOND and LAURA H. SMITH, Am. J. Psychiat. **92**:17 (July) 1935.

This paper represents a report made subsequent to the publication of a book by one of the authors (Bond, Earl, D., and Appel, K. E.: The Treatment of Behavior Disorders Following Encephalitis, New York, Commonwealth Fund, Division of Publications, 1931). In the present communication the authors discuss the kinds and the results of treatment on the basis of the findings in a survey of eighty-five children with postencephalitis, who were admitted to the Franklin School of the Pennsylvania Hospital in the last ten years. After discussion of the different methods used in the school until 1933 (strict hospital routine, modified hospital routine and easy boarding-school routine), the authors express the belief that the constructive restrictive boarding-school routine, with the teacher as the single executive, such as is used at present in the school, yields the best results.

An analysis of the eighty-five cases shows that the results were good in twenty cases and poor in fifty-six and that nine children are still at the school. A tendency to improvement in behavior, from moderate ability to get on with others to complete social adjustment, was shown by eighty of the eighty-five children. There were three cases of parkinsonism and three deaths (one from abscess of the brain, one from pneumonia and one from an unknown cause). Many children showed marked improvement on discharge from the school but could not (apparently) overcome the undesirable environment to which they returned. (A truant is a good boy running away from a bad school.) Many, however, have made and are maintaining excellent adjustments for several years. JAHR, Omaha.

ENCEPHALOGRAPHIC STUDIES IN MENTAL DISEASE. M. T. MOORE, DAVID NATHAN, ANNIE R. ELLIOTT and CHARLES LAUBACH, Am. J. Psychiat. **92**:43 (July) 1935.

This study represents a series of 159 encephalograms taken in 151 cases of neuropsychiatric disturbance in adults. In practically all the cases of organic

psychoses, such as schizophrenia, manic-depressive psychoses and epilepsy with psychosis, the encephalogram showed deformity of cerebral architecture. In cases of dementia paralytica and schizophrenia an individual encephalographic pattern was yielded. In various groups of psychoses normal outlines were presented.

JAHR, Omaha.

THE RELATIONSHIP BETWEEN VARIOUS EMOTIONAL DISTURBANCES AND THE SUGAR CONTENT OF THE BLOOD. EDWIN F. GILDEA, VIRGINIA L. MAILHOUSE and DONALD P. MORRIS, Am. J. Psychiat. **92**:114 (July) 1935.

It is well known that in animals exciting states are accompanied by elevation in the blood sugar content. In man the reports on this phenomenon are conflicting, owing to, the authors believe, discrepancies in interpretation of the term "emotional state" and to other conditions at the time the specimens of blood are taken. To obviate this situation, the determinations recorded in this communication were adequately controlled. The results point to the fact that in the normal subject severe emotional states, such as fright and grief, are accompanied by elevation of the blood sugar content. Hyperglycemia does not occur during severe emotional states in patients with mental disease. The authors suggest that the presence of underlying anomalies of metabolism is the cause of this lack of sugar mobilization in times of emotional stress.

JAHR, Omaha.

ETIOLOGICAL FACTORS IN THE PRODUCTION OF NEUROSES AND THEIR TREATMENT. SAMUEL Z. ORGEL, Arch. Pediat. **52**:325 (May) 1935.

This article is one of the many appearing on this subject, which seems to add nothing new.

WADDELL JR., University, Va.

THE MENTALLY DEFECTIVE CHILD. T. B. CUNNANE, California & West. Med. **43**:32 (July) 1935.

Cunnane presents observations made in a private school for defective children for a period of twelve years. He discusses common problems in the handling of the children and stresses the importance of proper segregation, habit training and modification of environment.

MARSHALL, San Francisco.

INTELLIGENCE TESTS ON NORMAL AND RACHITIC RATS. ANNELIESE FEST, Monatschr. f. Kinderh. **63**:445, 1935.

The intelligence of normal and rachitic rats was compared in respect to the time and the route taken by them to get to their food. A simple labyrinth was used. No difference was noted between the two groups.

GERSTLEY, Chicago.

Diseases of the Genito-Urinary Tract

CLINICAL STUDY OF THE SPERMATOGENESIS OF UNDESCENDED TESTICLES. DONALD W. MACCOLLUM, Arch. Surg. **31**:290 (Aug.) 1935.

This paper is based on a study of a group of patients with either unilateral or bilateral undescended testicles observed at the Children's Hospital in Boston, from 1900 to 1934. During this period six hundred and sixty-five patients with cryptorchidism were observed. The purpose of the study was to compare the degree of fertility of persons with cryptorchidism with that of normal persons. As orchiopexy had been performed on many of these children the author wished to determine whether spermatogenesis was normal after the child reached adult life. It was possible to make studies of fertility on eighty-nine men with undescended testicles. Three definite conclusions were reached: (1) The fertility of all persons with cryptorchidism seems to be lower than that of the normal person; (2) the cosmetic result following orchiopexy cannot be used as a criterion

of fertility, and (3) the percentage of definite fertility in persons who had undergone orchiopexy was computed to be 77 per cent, as compared with the estimated 10 per cent for persons with undescended testicles who had not undergone orchiopexy. In the opinion of the author orchiopexy is justified.

KAISER, Chicago.

EFFECT OF ANTERIOR PITUITARY-LIKE PRINCIPLE FROM THE URINE OF PREGNANCY ON UNDESCENDED TESTES IN MAN. B. WEBSTER, J. A. M. A. **104**:2157 (June 15) 1935.

Reports of clearly defined cases of cryptorchidism in which the patients responded successfully to the administration of extracts of the urine of pregnancy have caused considerable skepticism among physicians. This is a report of eleven patients so treated. In ten, descent of the cryptorchid testes occurred during the period of treatment. There was no response in the excretion of male hormone after therapy was instituted.

BONAR, Salt Lake City.

ACACIA IN THE TREATMENT OF NEPHROSIS. M. W. DICK, E. WARWEG and M. ANDERSCH, J. A. M. A. **105**:654 (Aug. 31) 1935.

The use of acacia intravenously in the treatment of edema due to nephrosis is based on the fact that acacia is an inert colloid which, when added to the blood, raises the osmotic pressure of the blood to a level above which edema occurs. The authors found its use disappointing. The effect was only transient or slight, and continued use of the gum led to marked lowering of the level of serum protein and to the development of enlargement and tenderness of the liver. When acacia therapy was discontinued the serum protein content tended to remain low, and the liver slowly resumed its normal size. In two patients acacia was noted in the edema fluid, and at autopsy in another case deposits were observed in the liver, lungs, kidneys, spleen, lymph nodes and bone marrow. The cause of the lowered protein content of the serum after administration of the preparation could not be explained. The authors conclude that the use of acacia in patients with nephrosis was of no value and gave undesirable results.

BONAR, Salt Lake City.

STRICTURE OF THE URETER IN CHILDREN: REPORT OF CASE. EDWARD S. POMEROY, Northwest Med. **34**:178 (May) 1935.

Pomeroy reports a case of pyuria of five and one-half years' duration in a girl of 8 years. Ureteral catheterization showed obstruction of the left ureter to a no. 6 catheter about 1 cm. from the bladder, but this was passed by a no. 4 catheter. A retrograde pyelogram showed stricture at this point and dilatation above it. Colon bacillus was obtained on culture. Treatment is being pursued according to the "four point" method of Crance (*J. A. M. A.* **104**: (Jan. 26) 1935).

SCOTT, Philadelphia.

VASCULAR CHANGES IN THE GLOMERULI OF THE KIDNEY AND THE EFFECT ON THE OTHER STRUCTURES OF THE NEPHRON. L. A. TURLEY and WILMA J. GREEN, South. M. J. **28**:773 (Sept.) 1935.

The author found that various kinds of vascular disease were present in the glomeruli of reduced kidneys. In some cases the lesions were focal, and although the foci were numerous, many capillary loops were still unaffected, allowing a sufficient blood supply to extraglomerular structures. In some cases most or all of the loops were affected, so that the blood supply to the extraglomerular structures was reduced or completely cut off.

The tubular lesion resulting from glomerular lesions was atrophy of the epithelium. The effect of the glomerular lesions on the extraglomerular structures

was in proportion to the reduction of the efferent blood supply. The important factor is not the kind but the extent of the glomerular lesions. Whenever the blood was prevented from passing through the glomeruli, regardless of the cause, the tubules atrophied in proportion to the reduction of the blood supply.

SCHLUTZ, Chicago.

THE EFFECT OF EXPERIMENTAL INTERFERENCE WITH THE BLOOD-SUPPLY OF THE KIDNEYS, WITH PARTICULAR REFERENCE TO THE FORMATION OF STONES. J. GRAY, Brit. J. Surg. **23**:458 (Oct.) 1935.

On the basis of the theory of Leriche and Policard, which states that "deposition of calcium takes place in connective tissue of low metabolism if the blood supply be diminished, particularly in the presence of hypercalcaemia," the following experiments were done:

One group of rabbits were placed on a normal diet, while another group were given a diet to produce hypercalcemia by the addition of calcium oxide and viosterol. The rabbits on both diets had the blood supply of the kidney reduced. Among the control group stones formed in 15 per cent, while among those on the high calcium diet stones formed in 45 per cent. These stones occurred in the ligatured side of the pelvis. No gross defect in renal function was produced by the procedure, and the urine from the ligatured side was alkaline in reaction. In cases in which stones were present the pelvic epithelium was abnormal, and stones could be demonstrated forming around the desquamated epithelium. The last finding is suggestive of the influence of lack of vitamin A on the pelvic epithelium.

SUMMERFELDT, Toronto, Canada.

PROGNOSIS OF HEMORRHAGIC NEPHRITIS. P. NOBÉCOURT, Bol. Soc. cubana de pediat. **7**:217 (June-July) 1935.

The immediate prognosis in hemorrhagic nephritis is generally good; the ultimate or later prognosis is uncertain. Slight albuminuria may persist for a long time. The condition may merge into chronic nephritis.

The values for the total chlorides are increased over those for the plasma chlorides at the beginning. Cardiovascular symptoms are rare. The urinary symptoms are characteristic: The volume of urine increases rapidly, and the albumin content diminishes. Hemorrhage may persist four or five months, and the albuminuria may persist even beyond that period. The focus of infection is practically always in the pharynx.

SCHLUTZ, Chicago.

PRECOCIOUS PUBERTY AND HYPERGENITALISM. FERNANDO MANRIQUE ZUNZUNEGUI, Pediatría españ. **24**:313 (Aug.) 1935.

There are four common forms of precocious puberty: the pineal, in which there is involvement of the pineal gland, with accompanying nervous disorders; the hypopituitary, which is commonly associated with a tumor at the base of the cerebrum; the adrenal, with adenoma of the cortex, hirsutism and hypertrichosis, and finally, the genital.

SCHLUTZ, Chicago.

A RARE CONGENITAL DEFORMITY OF THE GENITAL APPARATUS. EUGENIO SISTO HONTÁN, Pediatría españ. **24**:344 (Sept.) 1935.

The author reports a unique anatomic defect of the genitals in a boy 3 years old. It consisted in the misplacement of a small rudimentary penis in the perineum between the anus and the scrotum. The latter was fully developed, containing both testicles, and was in the proper location below the pubis, but anterior to and above the penis. The urethra, aside from partial hypospadias, was normal and functioned properly. The general development of the child was unusually good.

The author could find no report of a similar case in the literature.

SCHLUTZ, Chicago.

CONGENITAL CYSTIC KIDNEYS AND BLOOD PRESSURE. H. WILLER, München. med. Wchnschr. **82**:1437 (Sept. 6) 1935.

Five patients between the ages of 53 and 65 years with congenital cystic kidneys came to autopsy. The history failed to reveal symptoms referable to renal injury until just before death in four cases. One patient had symptoms for three years before death. All the patients died in uremia. Three did not have an elevation of the blood pressure or hypertrophy of the left side of the heart, and the other two had a systolic pressure of 160 mm. of mercury. In all the cases little renal parenchyma was present.

BRAHDY, Mount Vernon, N. Y.

CHRONIC INFECTIOUS DISEASES OF THE URINARY TRACT IN CHILDHOOD. A. SUNDAL, Acta pædiat. (supp. 3) **17**:1, 1935.

This contribution to the clinical pathology of chronic infection of the urinary tract is 124 pages long; there are 72 pages of discussion and 52 pages of case reports. Twenty-eight roentgenograms are excellently reproduced. The bibliography lists 121 references.

Sundal does not discuss the symptomatology of chronic infections of the urinary tract. He sets out to answer the following questions: What makes certain urinary infections chronic? Why are some patients benefited by medication, while others fail to improve with the same remedies? Does this difference in the therapeutic result depend on the presence of anatomic malformation of the urinary tract? If so, is it important whether the anomaly is one-sided or bilateral?

To provide an answer to these questions it was necessary to study the normal morphology of the urinary tract and renal function in children. The morphologic investigations were carried out by means of intravenous urography; the studies of function embraced determinations of the blood urea, tests of the concentrating power of the kidneys and tests for creatinine tolerance. The author describes an original modification of the latter. The normal values for the systolic blood pressure in children were also determined, 1,932 persons between 3 and 15 years of age being used as subjects. The pathologic material comprised 36 children from 3 months to 12½ years old. There were 8 boys and 28 girls. All had pyuria which had lasted, with or without remission, for weeks or years. The urinary tract was visualized by intravenous urography alone; retrograde pyelography was not employed. The function of the kidneys was tested in all the patients.

Of the 36 patients, only 6 had an entirely normal urinary apparatus. In 30 patients anomalies of greater or less degree were demonstrated; in 12 patients the variation from the normal was so slight as to be of questionable importance. Renal lithiasis was discovered twice and tuberculosis of the kidneys once.

Anatomic deformity is the most important of the factors which determine the duration of infection of the urinary tract. In the absence of demonstrable anomalies of the renal pelves, the ureters or the bladder, acute pyuria tends to subside promptly and is influenced favorably by medicaments given orally. If minor anatomic anomalies are present, the prognosis is doubtful. If the deformity is severe, complete recovery is not to be expected without surgical intervention.

These deformities are probably congenital in origin. Aside from the two patients with obstruction due to stone and one patient with renal tuberculosis, the series studied revealed no evidence that the lesions were acquired or that they depended for their existence on the presence of infection.

Chronic urinary infection is frequently associated with diminished renal function, even in the absence of a demonstrable anatomic anomaly; if obstruction is present, renal damage is the rule. If the infection is limited to one side, the functional capacity of the kidney on the opposite side is likely to be normal. In some patients renal insufficiency may precede recognized infection.

MCCUNE, New York.

Diseases of the Ductless Glands; Endocrinology

ARTERIOSCLEROSIS IN DIABETES: I. RELATIONSHIP BETWEEN PLASMA CHOLESTEROL AND ARTERIOSCLEROSIS. II. EFFECTS OF THE HIGH CARBOHYDRATE-LOW CALORIE DIET. I. M. RABINOWITCH, Ann. Int. Med. **8**:1436 (May) 1935.

Of persons who have had diabetes for five years or more, regardless of the age or of the severity of the disease, Rabinowitch found that more than 80 per cent have cardiovascular disease. He believes that the use of diets of low carbohydrate and high fat content is responsible for premature development of arteriosclerosis.

Excess plasma cholesterol is an important contributing factor in the production of arteriosclerosis. Reasons for this statement are discussed.

Diets high in carbohydrate and low in calories delay the development of cardiovascular disease by producing an immediate and sustained decrease in the plasma cholesterol content. Whether such diets actually prevent premature arteriosclerosis is not known.

In order that other data may be comparable with his, Rabinowitch suggests that the combined method of detecting arteriosclerosis be used in every case. This includes a careful physical examination; examination of the fundi; roentgen examination of the lower extremities for calcification of the arteries and roentgen examination (with a 6 foot [182.8 cm.] roentgenogram) of the heart. For estimation of the plasma cholesterol content samples of blood should be collected while the patient is in the fasting state.

READING, Galveston, Texas.

DIABETES INSIPIDUS: TREATMENT WITH INTERMEDIN AND PITMELANIN. HENRY H. TURNER, Endocrinology **19**:275 (May-June) 1935.

The treatment of diabetes insipidus presents many difficult problems, since solution of posterior pituitary, one of the most effective agents, often has undesirable secondary reactions, particularly in its pressor and gastro-intestinal effects. In addition to the oxytocic and the pressor fractions derived from the posterior pituitary gland, another has been obtained from the pars intermedia (Zondek and Krohn, 1932), which was named intermedin. This substance has a melanophoric effect on Phoxinus laevis.

Turner reports his results from the use of intermedin in five cases of diabetes insipidus, and his results from the use of pitmelanin (a melanophore-stimulating principle from the posterior lobe) in one case. One of the patients was a child 2½ years old, who had had polydipsia and polyuria since birth and who was drinking 2 gallons (about 4 liters) of water a day.

A reduction in diuresis and thirst occurred in all the patients, although the response was not so great as that obtained from equal amounts of solution of posterior pituitary. The patients preferred intermedin and pitmelanin to other pituitary preparations because of their freedom from pressor effects. In one case the symptoms were controlled by the oral administration of posterior pituitary substance. The preparations of intermedin and pitmelanin used by the author have thus been shown to contain the antidiuretic factors of the hypophysis and are of value in controlling the symptoms of diabetes insipidus.

JACOBSEN, Buffalo.

IDIOPATHIC HYPOPARATHYROIDISM AND TETANY IN THE FOWL. F. B. HUTT and W. L. BOYD, Endocrinology **19**:398 (July-Aug.) 1935.

A young pullet, which was apparently normal at 7:30 a. m., was found at 9 a. m. in convulsions and with the legs paralyzed. The common causes of paralysis in the fowl—(1) neurolymphomatosis gallinarum, a practically incurable disease usually accompanied by lesions of the sciatic nerve, (2) polyneuritis resulting from deficiency of vitamin B and (3) exhaustion of the bird's storage of vitamin D—could all be ruled out in this case.

A calcium content of 9.47 mg. per hundred cubic centimeters of blood plasma (the normal for a laying hen is 20 mg.) indicated tetany. The pullet had recently laid eleven eggs, and it is suggested that temporary idiopathic hypoparathyroidism at a time when there was a great demand for calcium resulted in tetany. Liberal doses of calcium gluconate given intraperitoneally and intravenously had no effect, and by the fifth day paresis persisted and coma had set in. Recovery was rapid when parathormone was administered. Egg-laying was promptly resumed, and the blood calcium content was raised to and maintained at 21 mg.

This is apparently the first case of tetany reported in birds.

JACOBSEN, Buffalo.

SOME PRACTICAL CONSIDERATIONS IN THE MANAGEMENT OF JUVENILE DIABETES. RUSSELL RICHARDSON and MORRIS A. BOWIE, M. Clin. North America **19**:273 (July) 1935.

The management of diabetes in the child differs in several important respects from that of the disease as it appears in adults. The basal metabolic requirement is variable and must be considered in outlining the dietary treatment. The rapid growth and usual activity of the young child must also be provided for by extra caloric intake. His requirements of protein for maintenance and growth are greater than those of the adult, and in addition he needs adequate amounts of calcium (at least 1 Gm. per day), besides iron and iodine.

Strict dietary regulation is imperative but may be made simple in its application, usually without the use of scales. Relatively high ratios of carbohydrate in the diet increase palatability but must be strictly prescribed. The low carbohydrate and high fat diet is not advised.

The amount of insulin required will be governed by the severity of the diabetes, the character of the diet and the extra quota of food necessary to provide for growth and development.

In the child diabetes also presents a variety of psychologic problems the management of which is an important part of the treatment. The home atmosphere should be that of encouragement, and segregation at meal time should be avoided. Family eating habits may at times be modified with benefit to both the patient and the family. The usual activities and play of childhood may be allowed. At school some responsible person should be made cognizant of the child's condition and requested to report any unusual symptoms which might appear and to discourage dietary irregularities. Sympathetic understanding and encouragement will work wonders in developing pride, self-reliance and the cooperation most necessary to the successful control of the disease.

EUGENE SMITH, Ogden, Utah.

THYMUS SUPERSTITION. HENRY W. HUDSON JR., New England J. Med. **212**:910 (May 16) 1935.

Autopsies in the Boston Children's Hospital during the period Jan. 1, 1930, to Sept. 1, 1934, revealed no deaths attributed to the thymus. In another institution, 11,000 tonsillectomies were performed, with no death attributable to the thymus. Replies to a questionnaire sent to outside pediatricians, otolaryngologists and surgeons also do not support the contention that the thymus may be a cause of sudden death in infants and children. Practically all stated the belief that taking roentgenograms of the thymus preoperatively as a routine measure is unnecessary.

GENGENBACH, Denver.

CARCINOMA OF THE THYROID GLAND IN CHILDHOOD WITH REPORT OF CASE. A. BRIAN TAYLOR and B. M. WILKINSON, Arch. Dis. Childhood **10**:99 (April) 1935.

The rarity of carcinoma of the thyroid in children is noted, and a review of the literature is given. Two types of tumors appear to occur: one relatively benign

and slow-growing and usually of the adenomatous type histologically; the other rapidly malignant, readily metastasizing and of the papilliferous type histologically.

An example of the second type in a girl of 6 years is described in detail. The multiple pulmonary metastases seen by means of the roentgen rays before the original growth became evident strongly suggested miliary tuberculosis. Later, when this was clinically untenable, the thyroid tumor appeared and caused rapid respiratory obstruction, with death from asphyxia four months after the first symptoms of the illness.

KELLY, Milwaukee.

MALIGNANT DISEASE OF THE LIVER. ? SECONDARY TO A SUPRARENAL TUMOUR. J. H. GIBBENS, Proc. Roy. Soc. Med. **28**:1327 (Aug.) 1935.

A girl of 4 years was brought to the hospital with a complaint of wasting and frequent abdominal pain that had been present for eight months. There was no vomiting. The bowels were regular and the appetite capricious. On examination gross enlargement of the liver, which extended to the umbilicus, was found. The surface was smooth, and the edge was regular. There was tenderness over the organ. Halfway between the umbilicus and the left costal margin a small, stony-hard mass could be felt on deep palpation. The spleen was enlarged. There was also a large mass of palpable glands above the left clavicle. The blood picture and roentgenograms of the chest and gastro-intestinal tract after a barium sulfate meal showed nothing abnormal. The Wassermann reaction and the Mantoux reaction were negative. During the six weeks' stay in the hospital the child wasted steadily, and the glands increased in size.

NOTE.—The patient died, and at postmortem examination an enormous mass of malignant tissue was observed in the right kidney. On section this proved to be round cell sarcoma. Masses which were malignant glands were observed in the mesentery, in the portal fissure and above the left clavicle. The enlargement of the spleen felt during life was due to a mass of malignant glands in the neighborhood of the spleen. There was no enlargement of the liver, the "enlargement" felt during life being due to the malignant glands in the portal fissure. The adrenal glands were not involved.

WILLIAMSON, New Orleans.

A COMPARISON OF THE PITUITARY BASOPHILIC SYNDROME AND THE ADRENAL CORTICO-GENITAL SYNDROME. F. G. LESCHER and A. H. T. ROBB-SMITH, Quart. J. Med. **4**:23 (Jan.) 1935.

A case of carcinoma of the adrenal cortex occurring in a woman 35 years of age showed all the major and many of the minor findings which Cushing has ascribed to adenoma of the basophil cells of the anterior lobe of the pituitary body.

The report contains a good review of these interesting endocrine disturbances, particularly emphasizing the comparison between the adrenal-corticogenital syndrome and the pituitary basophilic one.

BRADFORD, Rochester, N. Y.

SCHÜLLER-CHRISTIAN SYNDROME; LIPOID GRANULOMATOSIS WITH DEFECTS IN THE BONES, EXOPHTHALMOS, AND DIABETES INSIPIDUS. F. L. HORSFALL JR. and W. R. SMITH, Quart. J. Med. **4**:37 (Jan.) 1935.

A case of Schüller-Christian syndrome occurring in a boy of French-Canadian extraction was studied thoroughly by the authors at the McGill University Clinic in Montreal.

Pathologic studies revealed granulomatous lesions containing large quantities of lipoids. Cholesterol predominated by fractional chemical analyses of the lipoids in the lesions.

The authors collected fifty-nine other instances of the disease from the literature, and the reports of thirty-six of these were analyzed for a basis on which the present discussion is founded. Excellent plates illustrate the report.

BRADFORD, Rochester, N. Y.

HYPOPHOSPHATEMIA FROM EPINEPHRINE AND THE MECHANISM OF ITS PRODUCTION. V. ANGELINI and F. RASI, Riv. di clin. pediat. **33**:1019 (Sept.) 1935.

Observations were made on the blood chemistry of twelve healthy children before and after the subcutaneous injection of epinephrine hydrochloride. Thirty minutes after the injection the blood sugar content showed a mean increase of from 0.095 to 0.188 per cent. Simultaneously with this increase in the blood sugar content there was a mean diminution in the content of the inorganic acid-soluble phosphorus of 1 mg. per hundred cubic centimeters in the blood serum and of 0.7 mg. per hundred cubic centimeters in the whole blood. With the fall in the inorganic phosphorus content there is a corresponding increase in the value for the organic acid-soluble phosphorus of the blood, the content of the total acid-soluble phosphorus in the blood, being but little changed. Observations made three hours after the injection of epinephrine hydrochloride showed that the blood sugar content and the blood phosphorus content were again normal.

The conclusion is drawn that the hypophosphatemia following the injection of epinephrine hydrochloride is due not to the passage of phosphorus from the blood but rather to a transformation of inorganic phosphorus to organic phosphorus.

HIGGINS, Boston.

HYPOTHYROIDISM IN ONE OF TWINS. N. FAXÉN, Acta pædiat. **17**:565, 1935.

Faxén adds the reports of two new cases of hypothyroidism in one of twins to the growing literature concerning this curious phenomenon. The first case is that of twin boys; in the second case the patients were girls. The obstetrical notes describing the birth of the boys stated that there was only one placenta but the membranes were not described. The official diagnosis in the hospital where the girls were born designated them as uniovular twins; again the membranes were not described. In the first case, one of the twins exhibited a congenital goiter; he developed features characteristic of hypothyroidism during the first few months of life. One of the girls showed moderate but definite hypothyroidism from the neonatal period. In both cases the other twin was entirely normal in appearance and behavior and developed normally. Both of the handicapped infants responded well to the administration of a preparation of thyroid gland, although the goiter in the girl became only slightly smaller.

MCCUNE, New York.

EXOPHTHALMIC GOITER IN A GIRL FIVE YEARS OLD. GERDA BIILMANN, Hospitalstid. **78**:238 (Feb. 26) 1935.

After reviewing the statistics in the literature the author describes a typical case of exophthalmic goiter in a girl, 5 years of age. The condition had its onset at about the age of 3½ years. Both the father and the mother had thyroid disease. Besides the classic clinical symptoms, this patient presented an increase of growth in height, marked early ossification of the carpal bones and premature dentition.

ELGHAMMER, Chicago.

HEMORRHAGES DURING DIABETES MELLITUS, ESPECIALLY AFTER INJECTION OF INSULIN. A. C. M. LIPS, Nederl. tijdschr. v. geneesk. **79**:4879 (Oct. 19) 1935.

The author describes a case of hematemesis in the progress of diabetic coma in a boy of 18 years who two years before had hematuria after his first injection of insulin. In the cases described in the literature it is noted that the hemorrhages following the application of insulin are due not to insulin but to toxic changes of the blood vessels. The insulin or, in cases in which this was not given, trauma, embolism or thrombosis gave rise to hemorrhages.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Muscles, Bones, Joints and Lymph Glands

THE NATURE OF OSTEOGENESIS IMPERFECTA. ITALO D. PUPPEL, LOUIS E. BARRON and GEORGE M. CURTIS, Am. J. M. Sc. **190**:756 (Dec.) 1935.

Osteogenesis imperfecta occurring in a youth of 17 is reported. The following findings were present in this patient: blue scleras, increased osseous fragility, a history of fifty fractures, dwarfism, marked deformity and a decreased tendency to fractures since puberty. The calcium metabolism revealed no evidence of hyperparathyroidism. The calcium content of the serum, the phosphorus, the urinary excretion of calcium and the calcium balance were normal. The iodine content of the blood and the urinary excretion of iodine were increased. The chloride content of the plasma was near the low limit of normal, and the urinary excretion of chloride was normal.

It is stated that osteogenesis imperfecta does not appear to be due to hyperparathyroidism. It is suggested that this disease is due to congenital hypoplasia of the mesenchyma, perhaps associated with a deficiency in the production of bone phosphatase. Further study of the latter is desirable. HENSKE, Omaha.

SERUM PHOSPHATASE IN OSTEOGENESIS IMPERFECTA. O. NORRIS SMITH and JOHN M. MITCHELL, Am. J. M. Sc. **190**:765 (Dec.) 1935.

The origin, distribution and excretion of phosphatase and its rôle in normal persons are briefly reviewed. Among the cases of osteogenesis imperfecta reported in which studies of the phosphatase content of the serum were carried out an increase to an average level of about twice the normal content occurred in less than 30 per cent, chiefly in patients between the ages of 5 and 7 years. In the remaining 70 per cent the phosphatase content of the serum was within normal limits. This elevation is of more academic interest than clinical value at this time, as its mechanism is not yet understood. A severe case of oseogenesis imperfecta is reported, with notes on the clinical course (eighty-one days) and the observations at autopsy. HENSKE, Omaha.

HEMATOGENOUS OSTEOMYELITIS AND PYARTHROSIS DUE TO SALMONELLA SUIPESTIFER. J. B. WEAVER and L. SHERWOOD, J. A. M. A. **105**:1188 (Oct. 12) 1935.

Salmonella suipestifer, or the "hog cholera" bacillus, is now known to affect man occasionally, usually causing bronchopneumonia. Involvement of bones or joints apparently occurs only in infants, causing a mild disease of the epiphysis and extending toward the joint. The organism can be cultured from the local lesion but seldom from the blood. Agglutination reactions are positive. A case is described in a 9 month old girl. BONAR, Salt Lake City.

OSTEOMYELITIS IN INFANCY. WILLIAM THOMAS GREEN, J. A. M. A. **105**:1835 (Dec. 7) 1935.

Acute osteomyelitis in infants, contrary to the usual conception as derived from the same disease in older children, is more frequently due to Streptococcus haemolyticus. If the child survives the acute illness (the mortality is 21 per cent) recovery is rapid, and sequestration, recurrences and residual lesions are unusual. The mortality rate may be reduced by treating the acutely ill child first and not the lesion, which should be permitted to localize. Minimal surgical procedures should be followed rather than a poorly timed extensive operation which in the end jeopardizes the infant's life. BONAR, Salt Lake City.

DIAPHYSEAL ACLASIS. R. W. B. ELLIS, Proc. Roy. Soc. Med. **28**:1638 (Oct.) 1935.

A case of diaphyseal aclasis in a boy of 7 years is reported. At 12 months the mother noticed a hard lump at the upper end of the left tibia. Later, similar masses were noticed around the shoulders, wrists, knees and ankles. The mother

had a similar mass attached to her left clavicle. There were four other children in the family, none of whom was similarly affected. Roentgenograms showed the masses to be exostoses.

An account of the results of physical examination and pictures of the patient accompany the report.

WILLIAMSON, New Orleans.

OSTEOPSATHYROSIS; CONGENITAL OSSEOUS FRAGILITY OF LOBSTEIN. ROBERT CLÉMENT, Arch. de méd. d. enf. **38**:610 (Oct.) 1935.

The similarity between osteopsathyrosis and osteogenesis imperfecta has frequently been noted. The osseous fragility, with fractures affecting chiefly the diaphyses; the marked calcification and prompt repair; the irregularities in trabecular architecture, and the slate-blue sclerotics, are practically identical in both syndromes.

It is probable that these dysplasias represent different phases of the same disease, one being a frankly congenital form and the other, known as Lobsteins's disease, the delayed form, or *type tardive*. A case of the latter variety in a girl 3 years of age is described in considerable detail.

AMESSE, Denver.

RECOVERY IN A CASE OF CONGENITAL OSSEOUS FRAGILITY. JULES R. DREYFUS, Arch. de méd. d. enf. **38**:614 (Oct.) 1935.

The case of a boy, born March 28, 1934, is reported from the infant's clinic at the University of Bern. On the day of birth the mother observed a fracture of the left arm. On examination, on April 26, this fracture was found to be ununited. There was a family history of rickets, but no member had suffered from the usual triad of symptoms commonly associated with osseous fragility. Further investigation showed the infant to have marked craniotabes; there were a healed fracture of the left tibia, infiltration of the scrotal tissues and blue sclerotics. The Wassermann reaction of the blood was negative and the urine was normal.

Estimation of the calcium and the phosphorus content of the blood showed 9.4 and 3.02 mg., respectively, per hundred cubic centimeters. On April 29 the baby sustained a fracture of the right humerus; on May 3 there was a fracture of the left femur, and on May 9, a fracture of the right femur. Roentgenograms taken on May 23 revealed, in addition, fracture of both clavicles, of several ribs and of the left fibula.

Treatment consisted of the administration of 0.05 Gm. of cevitamic acid several times daily, followed by the administration of strontium lactate and liberal amounts of vitamin D. No further fractures were noted, and at the end of the year the infant could stand alone, but the inevitable deformities were readily apparent.

AMESSE, Denver.

SYNOSTEOSIS OF THE RADIOCUBITAL ARTICULATION. NÉGRIÉ and BARGE, Rev. d'orthop. **22**:678 (Nov.) 1935.

The authors report a case of synosteosis of the proximal articulation between the radius and the ulna. This synosteosis was congenital and involved the right arm in supination and the left arm in pronation. The upper 4 inches (10.2 cm.) of the bones were involved on each side.

The patient, a man aged 20 years, had been a fisherman since the age of 14 and had made several trips from France to Nova Scotia on fishing boats, carrying out his duties without disability. Supination and pronation of the forearms was done through rotation of the humerus at the shoulder joint.

Flexion and extension were not involved in either arm.

RYAN, Vancouver, Canada.

STILL'S DISEASE: A CLINICAL HISTOPATHOLOGIC CONTRIBUTION. S. LEVI, Riv. di clin. pediat. **33**:1214 (Nov.) 1935.

Reports are given of two cases of Still's disease. A careful histologic study was made of the various organs and tissues obtained at necropsy in one case.

The most characteristic changes are in the periarticular tissues and in the lymph nodes. In the periarticular tissues the fatty structure shows mucoid degeneration, and the lymph vessels show marked dilatation and proliferation of the walls. The involvement of the lymph nodes is generalized and characterized by dilated lymph vessels and an epithelioid or reticulo-endothelial transformation of the germinal centers; large basophilic and acidophilic cells are present.

Still's disease has a characteristic histopathology. It is not sufficiently specific, however, to permit of a definite diagnosis from histologic examination alone. The alterations occurring in Still's disease fit in with the conception of a chronic toxico-infectious stimulus which acts especially on lymphatic tissues, notably the germinative centers and lymph vessels.

HIGGINS, Boston.

FAMILIAL AND CONGENITAL ARTICULAR HYPERLAXITY. M. SCHACHTER, Arch. de pediat. d. Uruguay **6**:457 (Nov.) 1935.

Schachter reports three cases of articular hyperlaxity. The hyperlaxity was confined to the extremities and did not affect the skin. The disorder is familial and congenital. The etiology is obscure.

SCHLUTZ, Chicago.

ROENTGEN RAY TREATMENT OF GRANULOMA. G. SCHWARZ, Wien. Arch. f. inn. Med. **27**:353 (Sept.) 1935.

Schwarz has had very favorable results with the roentgen treatment of granuloma. In his formulation of the treatment he recommends the following procedure: Every lesion must be irradiated. The dose must be fractional and given in two day intervals. The field to be irradiated must not exceed 800 square cm. (24 by 30 cm., 18 by 40 cm., etc.). The dose must not exceed from 50 to 80 roentgens; at the most, 100 roentgens; that is, through a heavy filter, with a tension of 180 kilovolts, at a distance of 60 cm., the superficial dose should not exceed 250 roentgens.

The tolerance of the skin must be taken into account, as well as effects on the blood and the general systemic reaction, such as fever and nausea. The patient must be kept under constant observation, and any lesions that appear must immediately be treated. Sensitivity and the reaction vary a great deal in individual patients. The patient must avoid high altitudes.

SCHLUTZ, Chicago.

BENIGN GRANULOMATOSIS. FREDRIK SUNDELIN, Wien. Arch. f. inn. Med. **27**:437 (Sept.) 1935.

Granulomatosis generally occurs in young persons. It seldom appears before puberty, and the course is always chronic. The spleen is generally enlarged. extensive involvement of the pulmonary fields may take place without the appearance of serious signs. For this reason the disease is sometimes discovered by accident. The diagnosis is generally clear when the skin or osseous tissue is involved. The roentgenogram of the changes in the lung is typical in respect to the dense hilar shadows. A fan-shaped, thickly mottled density extends to the periphery. The processes may show progressive increase or stationary periods, and at times they may entirely disappear. There is generally a slight secondary anemia, and frequently there is leukopenia. A hygienic and dietetic regimen with the object of conserving the patient's strength is useful, as are the roentgen rays and arsenicals. The tuberculin reaction in these cases is almost uniformly negative.

It is generally believed that the disease is some rare or unusual form of tuberculosis or is a constitutional infection closely related to this disease.

SCHLUTZ, Chicago.

Diseases of the Eye

OCULAR HEADACHE. WEBB W. WEEKS, Bull. New York Acad. Med. **11**:487 (Aug.) 1935.

This article is part of the symposium on headache held at the State Meeting of the New York Academy of Medicine. The theories of the cause of headache of ocular origin are discussed. In 75 per cent of the cases ocular headache is due to eyestrain associated with the use of the eyes. The site may be supra-orbital, deep orbital, fronto-occipital or temporal. Unilateral supra-orbital headache is usually not due to eyestrain.

The local factors in headache of ocular origin are: disturbances in refraction and accommodation, disturbances in ocular motility, disturbances of retinal function and congestive states in and about the eyeball. These individual factors are discussed in detail.

JAHR, Omaha.

PARENTERAL INJECTION OF FOREIGN PROTEIN IN THE TREATMENT OF GONOCOCCAL OPHTHALMIA. J. B. HAMILTON, M. J. Australia **1**:772 (June 22) 1935.

Hamilton's experience with injections of sterile milk in the treatment of gonococcal ophthalmia has been favorable in adults when the temperature has been kept in a range of from 100 to 102 F., but his experience with children has been entirely disappointing. He lists certain definite contraindications to this treatment, which are: debilitation, particularly marasmus in children, tuberculosis, renal disease and pregnancy.

TENNEY, Madison, Wis.

CONGENITAL PARALYSIS OF ASSOCIATED LATERAL MOVEMENTS OF THE EYES WITH UNILATERAL FACIAL PARALYSIS. L. DUPUY-DUTEMPS, Ann. d'ocul. **171**:865 (Oct.) 1934.

Dupuy-Dutemps discusses a case of congenital paralysis of associated lateral movements of the eyes with unilateral facial paralysis in which convergence and associated vertical movements of the eyes were normal. The cause was probably agenesis of the nuclei of the sixth nerve and of the right facial nerve. It is unnecessary to explain these paralyses on the hypothesis of supranuclear centers. The oculomotor nuclei, with their connections, assure the coordination of the movements of the eyes.

BERENS, New York. [ARCH. NEUROL. & PSYCHIAT.]

INFANTILE TRAUMATISM ACCORDING TO DATA FROM THE OPHTHALMIC CLINIC OF THE KIEV INSTITUTE OF MEDICINE DURING TWENTY-FIVE YEARS. J. CHEVTCHOUK, Ann. d'ocul. **172**:457 (June) 1935.

Lesions of the eyes were twice as frequent in boys as in girls, and the objects that most frequently caused injuries were firearms, explosives, arrows and slingshots—dangerous playthings. The ages of the boys ranged from 8 to 14 years. In 90 per cent of the cases the globe was injured, and in 57.6 per cent there was perforation. In the majority of cases the lesions were of grave order. In view of this fact the question of such traumatism merits serious attention. It is necessary to give more attention to children's play and to their education. Reorganization of homes, schools and playgrounds is necessary, also grouping of school children for play according to their ages. Appropriate talks should be given to the children, parents and teachers by the school physician or oculist. The sale of dangerous toys should be prevented, and children should be supplied with and encouraged to use daily playthings that are interesting, rational and of low price.

MCKEE, Montreal, Canada. [ARCH. OPHTH.]

CONGENITAL PARESIS OF THE MOVEMENTS OF LATERALITY OF THE EYES TO THE LEFT. A. COLRAT, Rev. d'oto-neuro-opht. **12**:672 (Nov.) 1934.

The case studied was that of a boy, aged 9 years, with paresis of lateral movement of the eyes to the left, which was characterized by nystagmic movements

when the patient looked toward the left and by the impossibility of maintaining fixation of the eyes to the left. The automatic reflex movements were abolished or diminished. Congenital ocular paralyses occur in many forms, but no case analogous to the one reported has been found in the literature. As to the nature and seat of the lesion causing congenital paralysis of ocular movements, it is suggested that the anatomic lesion lies at the level of the nuclei of origin of the sixth pair or their fibers of projection.

DENNIS, San Diego, Calif. [ARCH. NEUROL. & PSYCHIAT.]

HEREDITARY CATARACT, ESPECIALLY CATARACTA CENTRALIS PULVURULENTA. A. RUSSO, Ann. di ottal. e clin. ocul. **63**:105 (Feb.) 1935.

Russo reviews previously reported cases of this type of cataract, which was first described by Vogt in 1921, and recalls the various theories concerning the pathogenesis of hereditary cataract and zonular cataract. He reports five cases of cataracta centralis pulvurulenta (embryonal nuclear cataract) in one family, the cases being studied especially with reference to the possible etiologic factors.

Three of the patients were the only sons of the first patient through marriage to a first cousin. The fifth patient was the only surviving brother of the first patient. The five children of this brother were examined, but none showed lenticular changes. The lens opacities in the first patient and his brother consisted in a sharply circumscribed mass of shiny points surrounding the embryonal nucleus and veiling the embryonal sutures. In the children similar central opacities were present, but, in a smaller central area, the white points were fused together in a peculiar formation resembling the foliage (*chioma*) of a tree. In all the cases the opacities were bilateral and similar in the two eyes. The peripheries of the lenses were clear, and the eyes showed no other abnormalities except myopia in one case and hyperopia or hyperopic astigmatism in the others. Vision was reduced from 2/20 to 9/10. Physical examination was in general without results. The blood calcium content was 8.8 mg. in one case, but in the other cases was normal or nearly so. Two patients showed signs of rickets, which in one was marked.

The factor of consanguinity in the inheritance of this condition is well illustrated by the normal children of the first patient's brother, whose marriage was not consanguineous. The cataract was inherited as a mendelian recessive which remained latent in this family while becoming manifest in the issue of the two cousins. Since the opacity in these cases is stationary, Russo questions whether it should be considered as cataract and suggests the name "central pulvurulent opacity."

GIFFORD, Chicago. [ARCH. OPHTH.]

TUBERCULOSIS OF THE CONJUNCTIVA. M. SORIA, Arch. de oftal. hispano-am. **35**:323 (June) 1935.

This condition occurred without any pathologic antecedents in a girl in excellent general health. The conjunctival lesion was apparently of only twenty days' duration and consisted of numerous hemispheric elevations of pinhead size, varying in color from wine red to yellowish red, which covered the tarsal conjunctiva. The preauricular gland was inflamed. The clinical picture was very much like that of Parinaud's conjunctivitis. A puncture of the inflamed preauricular gland yielded yellowish pus in which abundant tubercle bacilli were found. Inoculation of the peritoneum of a guinea-pig with the fluid from this gland and also with a fragment of the conjunctival lesions gave positive results. A histopathologic examination of the peritoneum showed tuberculous granulation tissue with numerous giant cells.

Roentgen examination of the chest revealed a typical fibronodular process. No examination for bacillemia was made. A complete cure was obtained with sodium aurothiosulfate, with a maximum dose of 0.25 and a total dose of 2.5 Gm., the body weight increasing 4 Kg.

The question arises whether in this case the process was primary or secondary

FINLAY, Havana, Cuba. [ARCH. OPHTH.]

FAMILIAL NEUROFIBROMATOSIS. K. T. A. HALBERTSMA, Arch. f. Ophth. **134**:167 (Aug.) 1935.

Halbertsma reviews the literature concerning ocular manifestations of neurofibromatosis (glaucoma, degeneration of the optic nerve, blastoma of the retina or of the optic nerve, neuroma of the lid) and reports the pedigree of a family in which three members of one generation and one member of the following generation were affected. The inheritance seemed to be, except for some irregularities, of the dominant type. KRONFELD, Peiping, China. [ARCH. OPHTH.]

HISTOLOGIC OBSERVATIONS IN A CASE OF FAMILIAL DEGENERATION OF THE CORNEA. J. URBANEK, Klin. Monatsbl. f. Augenh. **94**:382 (March) 1935.

A man aged 28 had presented familial degeneration of the corneas since his fourth year. His mother and grandmother suffered from the same affliction. His eyeballs were examined histologically after he succumbed to a fatal accident. It could be shown by divers methods of staining that the familial degeneration of the corneas consisted in deposition of fatty acids and their esters beneath the epithelium, where Bowman's membrane had been destroyed. The anterior elastic membrane was entirely absent in both eyes, which is contrary to the findings in E. Fuchs' case. STOLL, Cincinnati. [ARCH. OPHTH.]

RÔLE OF PARATHYROID GLANDS IN THE PATHOGENESIS OF CATARACTS IN YOUNG PERSONS. O. A. ROMANOVA-DUCHAN, Sovet. vestnik oftal. **6**:67, 1935.

Romanova gives a thorough review and analysis of the literature on the relation between the function of the parathyroid glands and cataracts of senile and young persons. In order to verify the various opinions on this relationship, he examined a group of twenty-two patients suffering from cataracts and a control group who were free from lens opacities. The ages of all but four patients varied from 9 to 30 years. Eleven patients had zonular cataracts, and eleven, secondary membranes and soft ones after extraction.

The patients were examined carefully by neurologists for symptoms of latent tetany. The blood serum was examined for its content of calcium and of potassium. The evidence for tetany was considered positive if Chvostek's, Trousseau's or Erb's phenomenon was present. The blood calcium was determined by de Waard's method and the blood potassium by the Kramer-Tisdall method. Since symptoms of tetany may be caused not only by a lowered level of calcium in the blood, but also by a change in the proportion of potassium to calcium, an increase in the index of the ratio of potassium to calcium was considered positive for tetany.

The average concentration of calcium in the blood of cataractous patients was 10.38 mg. per hundred cubic centimeters; that of potassium was 24.5 mg. In the control group the calcium was 11.06 mg. and the potassium 24.72 mg. per hundred cubic centimeters. A low level of calcium was found in six patients, or 27 per cent. Latent tetany was observed in six patients.

Thus the importance of hypofunction of the parathyroid glands in the pathogenesis of cataract in young persons was confirmed, as the symptoms of that condition were observed in about 50 per cent of the cataractous patients.

SITCHEVSKA, New York [ARCH. OPHTH.]

Skin Diseases; Allergy

ALLERGY TO ADHESIVE TAPE: REPORT OF TWO CASES. H. A. SLESINGER, Arch. Pediat. **52**:715 (Oct.) 1935.

Two cases of generalized dermatitis are described which, in the absence of other causative factors, are thought to be examples of allergy due to adhesive tape.

WADDELL JR., University, Va.

OBSERVATIONS ON THE NATURE OF THE HOUSE DUST ALLERGEN. MILTON B. COHEN, TELL NELSON and B. H. REINARZ, J. Allergy **6**:517 (Sept.) 1935.

Investigation carried on with cotton linters would indicate that the active substance in house dust is not a mold and is not dependent on bacterial or mold action on the linters.

The house dust allergen is probably a degenerative product produced during the aging process in cotton linters and other substances such as feathers and kapok.

HOYER, Cincinnati.

THE EFFECT OF POLLEN THERAPY UPON THE COMMON COLD IN HAY FEVER SUBJECTS. LOUIS STERNBERG, New York State J. Med. **35**:713 (July 15) 1935.

Fifty-three of two hundred patients suffering from hay fever were subject to frequent colds. After injections of pollen thirty-six of the fifty-three persons had relief from colds. The remaining seventeen, who were not relieved from colds, also received little relief from hay fever.

AIKMAN, Rochester, N. Y.

GASTRO-INTESTINAL ALLERGY; POINTS TO CONSIDER IN ITS DIAGNOSIS. MERLE W. MOORE, Northwest Med. **34**:200 (June) 1935.

The possibility of allergy as a cause of gastro-intestinal symptoms must be considered. About 44 per cent of allergic patients have a history of gastric symptoms. Faulty peristalsis has been visualized in cases of anaphylactic shock produced in rabbits. This has been observed in man by roentgen study after the eating of foods to which the patient is sensitive.

Pain may be caused by serous exudation into the visceral coats, by distention, by pseudo-obstruction and by hyperperistalsis. If the offending proteins are those existing in the food as eaten, the symptoms are usually largely gastric and make a prompt appearance, while if they are due to split products of protein digestion, they may come on only after some time and are usually of the lower abdominal type. While gastro-intestinal allergy manifests itself mostly at an early age, it may appear at any age by the patient suddenly becoming sensitive to a food which he had eaten all his life.

Wheat, milk and egg are the principal offending foods. The coincident occurrence of other allergic phenomena is of great value in diagnosis. Cutaneous reactions, if positive, are of value; if negative, they are of no value. The elimination diets of Rowe are useful in establishing the cause of the symptoms. Epinephrine is usually not of value in relieving pain, distention and other symptoms.

SCOTT, Philadelphia.

THE ALLERGIC CHILD. M. F. PETERSEN, West Virginia M. J. **31**:414 (Sept.) 1935.

This article is a brief discussion of allergy in infants and young children, with special reference to eczema and asthma. The usual causes and treatment of these two diseases are briefly reviewed. Nothing unusual is presented.

SHAWKEY, Charleston, W. V.

HISTOLOGIC EXAMINATION OF TUMORS OF THE SCALP AND GLANDS. P. ARMAND-DELILLE, J. BABLET and J. PORGE, Bull. Soc. de pédiat. de Paris **33**:22 (Jan.) 1935.

Histologic examination was made of material taken for biopsy, consisting of a tumor of the scalp and an inguinal lymph gland, as well as of a cervical gland and pieces of the liver and spleen removed post mortem. Detailed descriptions of the sections are given. Biopsy showed sarcomatous structure of both specimens, and

examination of the postmortem material, sarcomatous neoplasms as well as inflammatory changes. There was reticular hyperplasia with necrosis, which suggests tuberculosis, and numerous cocci were seen in the vessels, which makes the presence of staphylococcic septicemia possible. The diagnosis of lymphogranulomatosis and sarcoma of the bone marrow was eliminated, and the condition was considered to be malignant lymphoid tumor, that is lymphoblastic sarcoma or lymphocytoma. The child became progressively anemic before death.

BENJAMIN, Montreal, Canada.

ACUTE GENERALIZED PRURIGO. L. BABONNEIX and L. GOLÉ, Bull. Soc. de pédiat. de Paris **33**:30 (Jan.) 1935.

A boy, 4½ years old, was admitted to the hospital because of a generalized cutaneous rash consisting of tiny papules, many of which were covered by brownish hemorrhagic crusts; there were also a few vesicles present, especially behind the ears. He had fever for two days. No history as to the onset and course of the disease prior to his admission was obtained. It was considered most probable that the condition was generalized acute prurigo, possibly of toxic origin, which is usually accompanied by vesicles somewhat resembling those of varicella and which may not cause any itching when the condition occurs in a child.

BENJAMIN, Montreal, Canada.

CUTANEOUS ARGYRIA DUE TO OVERDOSAGE OF SILVER SALTS INGESTED OVER A PERIOD OF THREE YEARS. ALFRED CAYLA, Bull. Soc. de pédiat. de Paris **33**: 31 (Jan.) 1935.

Two brothers, 10½ and 8½ years old, respectively, presented a grayish discoloration of the skin and mucous membranes. They had been observed shortly before the appearance of this peculiar color, and no abnormality of the skin or mucous membranes was noted at that time. They had been given tablets containing silver salts for about fifteen days each month over a period of three years and in addition had drops of a silver preparation instilled in the nostrils frequently. The tablets had been prescribed by a physician three years previously when they had colitis, and the parents had continued to administer them, apparently with the idea of prophylaxis against digestive disturbance. The buccal mucosa showed a grayish discoloration except for a thin margin of the gums next to the teeth. It was estimated that each boy had ingested from 30 to 40 Gm. of metallic silver during the three years. Large doses of hyposulfite given by mouth, as well as a preparation containing iodine, were to be tried in an attempt to improve the condition. Apart from the discoloration of the skin and mucous membranes, which varied in intensity but was present over practically the entire body, no abnormal signs or symptoms were present.

BENJAMIN, Montreal, Canada.

INFANTILE ECZEMA. J. SÉDILLOT, Progrès méd., Jan. 4, 1936, p. 14.

In this article Sédillot reviews the history of the various interpretations of the eczematous process. He gives in considerable detail the exposition of Péhu and Woringer, which shows that the allergy in infants which leads to eczema is a "biophallergy," or an inherited condition.

LESLIE, Evanston, Ill.

ACRODYNIA. A. TEN BOKKEL HUININK, Nederl. tijdschr. v. geneesk. **79**:834 (March 2) 1935.

A case in a boy of 3½ years is described, in which convulsions were temporarily present and the psychic symptoms persisted for a long time.

VAN CREVELD, Amsterdam, Netherlands.

HEREDITY OF ALBINISMUS CIRCUMSCRIPTUS. J. SANDERS, Nederl. tijdschr. v. geneesk. **79**:1245 (March 23) 1935.

Three families consisting of seventy-four persons are described, in thirty-nine of whom albinismus circumscriptus occurred on the forehead, abdomen and legs. The anomaly is dominant. The hypothesis of Frassetto of the cause of this hereditary deviation is discussed. In the author's opinion, this hypothesis cannot explain the occurrence in all the cases.

VAN CREVELD, Amsterdam, Netherlands.

PSORIASIS AND MEASLES. C. H. BEEK, Nederl. tijdschr. v. geneesk. **79**:4157 (Aug. 31) 1935.

Through an investigation of the anamneses of 100 adults suffering from psoriasis and of 100 persons used as controls, it could be proved that in both groups there was a history of measles. This observation is contrary to the opinion that measles protects against psoriasis.

VAN CREVELD, Amsterdam, Netherlands.

TREATMENT OF FAVUS IN THE DERMATOLOGICAL CLINIC OF THE UNIVERSITY OF LEYDEN (NETHERLANDS). H. W. SIEMENS, Nederl. tijdschr. v. geneesk. **79**:5140 (Nov. 2) 1935.

The routine treatment of favus, practiced with satisfactory results, is described in detail. The main principles of the treatment are as follows: thorough examination of the whole family before starting treatment and simultaneous treatment of all the diseased members, epilation by means of roentgen irradiation, ablution with soap, ointment cap, induction of peeling of the skin by tincture of iodine, maintenance of alopecia by manual epilation and extensive clinical and microscopic control of the results.

VAN CREVELD, Amsterdam, Netherlands.

DERMATITIS GANGRAENOSA INFANTUM. I. COHEN, Nederl. tijdschr. v. geneesk. **79**:5143 (Nov. 2) 1935.

The description is given of a case of dermatitis gangraenosa in a baby 1 month old, who until ten days after birth had been healthy. In material obtained from a complicating closed cutaneous abscess only Staphylococcus aureus was observed. Notwithstanding the age, the progress of the ulcers and the serious general state of the child, recovery was obtained after two months' hospitalization, the most important therapeutic agents being numerous injections of antistaphylococcus serum and daily blood transfusions.

VAN CREVELD, Amsterdam, Netherlands.

Surgery and Orthopedics

ESSENTIAL HYPERHIDROSIS CURED BY SYMPATHETIC GANGLIONECTOMY AND TRUNK RESECTION. ALFRED W. ADSON, WINCHELL M. CRAIG and GEORGE E. BROWN, Arch. Surg. **31**:794 (Nov.) 1935.

The authors define essential hyperhidrosis as excessive perspiration that is aggravated by exposure to warm temperatures, by nervous excitement and by emotional strain. The anatomy, physiology and etiology are discussed. A study of their cases furnished strong evidence of an abnormality referable to the central nervous system in this disorder. The treatment employed was sympathetic ganglionectomy, which brought about a complete cure in the five patients operated on.

KAISER, Rochester, N. Y.

STUDIES ON ETHER DOSAGE AFTER PRE-ANESTHETIC MEDICATION WITH NARCOTICS (BARBITURATES, MAGNESIUM SULPHATE AND MORPHINE). FRANK A. CALDERONE, J. Pharmacol. & Exper. Therap. **55**:24 (Sept.) 1935.

After experimental study on dogs, Calderone came to the conclusion that "The margin of safety in ether anesthesia is neither increased nor decreased by preliminary medication with sedative doses of morphine or the barbiturates mentioned. It is lessened with magnesium sulphate. The advantage of giving morphine or the barbiturates lies in the mental and physical relaxation they produce."

PILCHER, Cleveland.

HEAD INJURIES: THEIR MANAGEMENT AND TREATMENT. TEMPLE FAY, South Carolina M. J. **31**:233 (Dec.) 1935.

The proper supply of fluid must be maintained in injuries to the head and comparative dehydration maintained. The objectives in treating a traumatic wound of the head are: first, to keep the patient alive and second, to reestablish the individual as an economic asset to the community.

Lumbar puncture is always done to relieve pressure. Surgical intervention is indicated only in cases of compound or comminuted fracture of the skull in which the fracture extends in the cerebral substance and causes pressure on important cerebral areas.

The treatment of shock is outlined. The use of a 50 per cent solution of dextrose and saline solution given intravenously is advised. Large doses of sodium phenobarbital are given to keep the patient quiet. The posttraumatic treatment is outlined, with emphasis on a "dry" diet, the amount of intake of fluid to be limited to 32 ounces (946.2 cc.) in twenty-four hours.

WESTON JR., Columbia, S. C.

BLOOD TRANSFUSION IN CHILDREN'S SURGERY. EMILIO GARCÍA PÉREZ, Bol. Soc. cubana de pediat. **7**:355 (Nov.) 1935.

The author discusses the widespread use of transfusion. He advocates the formation of a transfusion "team" which could be available on short notice. He considers surgical intervention a risk unless the mechanism for successful blood transfusion is available. Blood transfusion may be given before, during or after operation. Patients of all ages are suitable subjects. The method of Lindemann is particularly advocated.

SCHLUTZ, Chicago.

ANESTHESIA IN ORTHOPEDICS DURING CHILDHOOD. H. MÜNDTRATH, München. med. Wchnschr. **81**:1934 (Dec. 13) 1934.

Mündtrath advocates the intravenous administration of a barbital derivative for preliminary anesthesia. The dose for different ages varies from 1 cc. for an infant to 5 cc. for a child 14 years of age. Narcosis follows from ten to twenty minutes after the intravenous injection. The anesthesia is then completed with ether inhalation. There is no stage of excitement. After the operation the child sleeps longer and the postoperative vomiting is less than when ether inhalation alone is used.

BRAHDY, Mount Vernon, N. Y.

Teeth and Dentistry

DENTAL CARIES AND PARADENTAL DISTURBANCES: I. IMPORTANCE OF AN ADEQUATE DIET FOR HEALTH OF TEETH AND PARADENTIUM. HERMAN BECKS and NINA SIMMONDS, J. Am. Dent. A. **22**:1724 (Oct.) 1935.

The authors review certain of the outstanding publications on dental caries from the standpoint of dietary contributory causes and mention changes in the bony tissue in animals which were fed specially designed diets—one deficient in calcium and high in phosphorus, with no cod liver oil; another low in phosphorus and

high in calcium, with an adequate amount of vitamin D, and a third with a normal calcium and a normal phosphorus content, for control. In regard to the first diet, osteoporosis and osteodystrophia fibrosa were found to occur in dogs, while with the second a rachitic condition developed in rats. There was also partial degeneration of the odontoblasts. There appeared to be little evidence of osteoclastic activity.

There is a careful exposition of the method of obtaining information as to dietary habits from patients, together with suggested diets for use in appropriate cases. As a result of their examination of menus the authors feel that the average diet for human beings, especially from the ages from 10 to 12 and sometimes before this period is often nutritionally incomplete. They have frequently found a deficiency in calcium and phosphorus and, in some instances, in the vitamins. The protein content was also found to be below that commonly recommended. They raise the following question: "Are tooth decay and paradentosis in many instances the first and sometimes the only symptoms of such deficiencies?"

NOYES, Chicago.

DENTAL CARIES AND TUBERCULOSIS OF THE MEDIASTINAL LYMPH NODES. G. ROSENTHAL, Paris méd. **2**:235 (Sept. 28) 1935.

Rosenthal deplores the frequency with which dental caries in the deciduous teeth of children is neglected. He believes that the infection of the lymph nodes associated with dental decay render them particularly susceptible to infection with the tubercle bacillus. These bacilli are carried from local nodes to the mediastinal nodes, from which general dissemination may occur. LESLIE, Evanston, Ill.

ENDOCRINE DISTURBANCES AND LESIONS OF THE TEETH. A. WILCKEN, Progrès méd., Sept. 14, 1935, p. 1487.

Wilcken gives a brief review of instances of endocrine disturbance in which the teeth have been found to be affected. Puberty, pregnancy and lactation may be associated with decalcification. Thyroid deficiency is known to produce defects in the enamel, particularly in the temporary teeth. Parathyroid deficiency may bring in its wake dental caries. Tellier and Beyssac reported severe dental lesions in a case of hyperthyroidism associated with ovarian deficiency. Wilcken concludes his article with the following statement: "It is suitable to consider endocrine disturbances as being capable in certain cases of an unfavorable action on the dental system."

LESLIE, Evanston, Ill.

Miscellaneous

FEVER THERAPY IN GONORRHEAL ARTHRITIS AND CHOREA. TRUMAN G. SCHNABEL and FERDINAND FETTER, Ann. Int. Med. **9**:398 (Oct.) 1935.

The Kettering hypertherm was used in these studies. Eighteen adult patients with acute or chronic arthritis and eleven children with Sydenham's chorea comprised the series of patients.

Three children had severe attacks of chorea; six had moderately severe attacks, and in two the attacks were mild. The age of the patients varied from 4 to 15 years. The average number of treatments given was four. Each treatment consisted of three hours of elevated temperature. Six patients had associated mitral valvulitis. The other five children showed no evidence of cardiac involvement.

Of the eleven patients, nine were cured and have remained free from symptoms from one to six and one-half months following treatment. Two patients did not have complete cessation of their symptoms but showed distinct improvement. In all the cases the rapid improvement after the first or second treatment, with no other form of therapy, indicated that the fever was the effective therapeutic agent.

One patient, who was not included in the series reported, died as a result of fever therapy. Death occurred seventeen hours after treatment. Necropsy revealed intense cerebral edema and venous congestion. The authors ascribe the death to a disturbance of the heat-regulating mechanism.

This form of therapy offers the best chance of cure for both gonorrheal arthritis and chorea.

READING, Galveston, Texas.

THE RELATIVE EFFICIENCY OF A SERIES OF ANALEPTICS AS ANTIDOTES TO SUBLETHAL AND LETHAL DOSAGES OF PENTOBARBITAL, CHLORAL HYDRATE AND TRIBROMETHANOL ("AVERTIN"). O. W. BARLOW, J. Pharmacol. & Exper. Therap. **55**:1 (Sept.) 1935.

In a series of 1,600 experiments on adult albino rabbits narcotized by pentobarbital, chloral hydrate and tri-bromethanol, Barlow found, among many other results, that "Artificial respiration especially with gas mixtures containing 5 to 10 per cent of carbon dioxide, is highly effective as a single resuscitation measure against lethal doses of these hypnotics. This procedure because of its safety and high degree of effectiveness after paralysis of the respiratory center is considered to be of outstanding usefulness either alone or in conjunction with other analeptic measures."

Ephedrine was useful in moderating the effects of tri-bromethanol or of chloral hydrate, but too large doses of it may add to the depression.

Caffeine was scarcely effective in doses larger than commonly used therapeutically, and in still larger doses it added to the depressant action of the narcotics.

PILCHER, Cleveland.

Society Transactions

AMERICAN PEDIATRIC SOCIETY AND CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

Joint Meeting, Bolton Landing, Lake George, N. Y., June 11-13, 1936

FRITZ B. TALBOT, M.D., *President, in the Chair*

HUGH MCCULLOCH, M.D., *Secretary*

First Session

Thursday Afternoon, June 11

BASAL METABOLISM OF GIRLS: PRESIDENT'S ADDRESS. DR. FRITZ B. TALBOT, Boston.

This paper was published in the AMERICAN JOURNAL OF DISEASES OF CHILDREN (**52**:1 [July] 1936).

INTESTINAL STASIS DUE TO LOW INTAKE OF MINERALS. DR. ELIZABETH CHANT ROBERTSON, Toronto, Canada.

This paper will be published in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

A CASE OF OSTEOSCLEROSIS FRAGILIS (ALBERS-SCHÖNBERG DISEASE). DR. BENJAMIN KRAMER and DR. BÉLA HALPERT (by invitation), Brooklyn.

The clinical manifestations of osteosclerosis fragilis (marble bones) in the adult are so mild that the diagnosis is seldom made without the aid of the roentgenologist, and the patient suffers little discomfort except for an occasional fracture which usually heals promptly. In the infant and in the child the clinical symptoms are striking and characteristic, and the outcome is usually grave, so that no one who has once observed a case could fail to recognize a second one. Although McCune and Bradley were able to collect 65 instances of this condition, to which they added 1 of their own, the number of complete autopsies in their series was only eight. Our case report includes a description of the clinical study of the patient, with a complete account of the necropsy and quantitative chemical studies of the bones. Our patient was a 4½ month old boy who presented the classic picture of retarded mental and physical development, macrocephaly, bilateral primary atrophy of the optic nerve, skeletal changes simulating those found in rickets, hepatomegaly and splenomegaly, progressive secondary hypochromic anemia with thrombocytopenia and striking roentgen changes in the bones.

These roentgen findings in the bones of the extremities were remarkably uniform. The shafts of the long bones were represented by a dense shadow that filled the entire shaft but retained the normal contour of the bone. On its distal and proximal ends each shaft was capped by a less dense shadow, structureless and irregular, which at times suggested the healing of rachitic metaphyses with probably a faint and incomplete line test. Definite cupping, fringing or spur formation was also present, with apparent slight epiphysial displacement. Between these less opaque shadows and the shaft proper there was a zone of rarefaction. This sequence of dense homogeneous structureless diaphysial shadows, zone of rarefaction and less dense irregular peripheral shadow obtained in all the bones. In the

centers of ossification there was a uniformly dense nucleus surrounded by a ring-like area of rarefaction, which in turn was surrounded by a less dense zone of deposition of calcium that distinctly outlined the carpal or tarsal bones. The metatarsal bones, on the other hand, showed localized dense shadows in the proximal and distal portions of the shaft. The bone itself was capped by a less dense shadow.

At the base of the skull all the bones were uniformly dense. No diploic structure was visible, nor was there any cellular structure in the mastoid. The clinoid processes were dense and rounded or absent, and the sella turcica seemed small.

Roentgenograms taken post mortem showed the same changes in the bones, except that they seemed to be more definite. Specimens of bone from the ribs, the skull and the long bones of the extremities were obtained for histologic examination and chemical analysis.

The chemical studies of the blood serum showed a total serum protein content of between 5.2 and 5.5 mg. per hundred cubic centimeters, with an albumin-globulin ratio of 1.41. The calcium content varied between 7.8 and 8.8 mg., and the phosphorus content, between 2.6 and 3.1 mg. The phosphatase units, determined by the Bodansky method, on first examination were 23, and twenty-four days later were 28.5. One month of intensive antirachitic therapy with viosterol and halibut liver oil, given by mouth, supplemented by ultraviolet irradiation, had no effect on the bone or on the composition of the blood serum.

Chemical analysis of the bones showed a moderate increase in ash, both found and calculated, above that obtained in a normal child of 2 months reported by Wells, a striking constancy of the residual calcium-phosphorus ratio in all the bones of from 1.93 to 1.96, an increased content of calcium carbonate over the total calcium content and a high fat content in the bones which one could hardly suspect from their histologic appearance.

The characteristic change in the long bones seemed to be a diffuse injury resulting in a persistence of the provisional cartilage, producing widening of the cartilage plate and irregularity of the chondro-osseous junction, with remnants of calcified cartilage matrix in the trabeculae. The latter were abundant and replaced the bone marrow cavity but were made of imperfectly formed bone. The bone marrow for the most part was replaced by loose connective tissue. In some places this was composed of masses of connective tissue in which fragments of bone trabeculae were embedded. Hemorrhage into the bone marrow in some places and islands of new blood cell formation were present. Intensive fragmentation of newly formed bone trabeculae was present in the submetaphysial zone, with innumerable large osteoclasts.

An encephalogram showed no abnormalities of the ventricular system.

DISCUSSION

Dr. Irvine McQuarrie, Minneapolis: I should like to ask whether the authors made any studies of the phosphatase of the blood or tissues.

Dr. Benjamin Kramer, Brooklyn: We reported phosphatase on one of the charts, showing that the phosphatase units were increased and remained uninfluenced by the antirachitic therapy. We have also taken sections of the cartilage and made studies of the phosphatase of the cartilage, but these are not yet completed.

A Comparison of the Antirachitic Effect on Man of Vitamin D from Different Sources. Dr. T. G. H. Drake, Toronto, Canada.

Observations on the antirachitic value of various amounts of cod liver oil, viosterol, irradiated fresh and evaporated milk, irradiated cholesterol and irradiated yeast have been made on 1,228 infants under home conditions over five winter months. Thirteen per cent of 244 infants who received no vitamin D showed moderate or marked rickets.

No evidence was obtained of any difference in the antirachitic effectiveness for man, rat unit for rat unit, of vitamin D administered in the form of cod liver oil, a mixture of high potency fish liver oils, irradiated cholesterol, irradiated fresh milk or irradiated evaporated milk.

No evidence was obtained of any great difference in the antirachitic effectiveness for man, rat unit for rat unit, of the aforementioned substances and viosterol.

The administration of vitamin D in amounts as low as 95 units daily prevented the development of rickets of a moderate or marked degree in every case. No evidence was obtained that this extremely small amount was a less effective antirachitic as measured by the roentgen rays than the larger amounts usually administered.

Rapid healing of rickets of a moderate or marked degree resulted from the daily administration of as little as 300 and 500 units of vitamin D. The 300 units were administered in the form of irradiated cholesterol and the 500 units in the form of irradiated yeast.

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COMPARATIVE VALUE OF COD LIVER OIL, VIOSTEROL AND VITAMIN D MILKS IN THE PREVENTION OF RICKETS AND CERTAIN BASIC FACTORS INFLUENCING THEIR EFFICACY. DR. MARTHA M. ELIOT, DR. E. M. NELSON (by invitation), DR. DONALD J. BARNES (by invitation), DR. FLORENCE A. BROWNE (by invitation) and RACHEL JENSS, Ph.D. (by invitation), Washington, D. C.

An investigation of the relative efficacy of several different forms and dosage levels of vitamin D was carried out in Detroit during the winter months of 1933, 1934 and 1935 with a view to testing the practical value of the various substances when administered to infants in their own homes.

The study was made by the United States Children's Bureau and the United States Food and Drug Administration with the cooperation and assistance of the Children's Hospital of Michigan, the Detroit Departments of Health and Welfare, the Children's Fund of Michigan and a number of hospitals that permitted access to their records of new-born infants.

Thirteen groups of infants were given an antirachitic substance. Four groups were given cod liver oil at dosage levels averaging approximately 270, 540, 675 and 810 U. S. P. units; three groups were given approximately 675, 1,350 and 2,025 units of viosterol, and six groups were given evaporated vitamin D milks, including yeast milk containing 400 or 170 units per reconstituted quart, milk to which cod liver oil concentrate had been added in the amount of 400 or 135 units, irradiated milk containing 150 units and milk to which viosterol had been added in the amount of 400 units per reconstituted quart.

The potency of all the substances was established by the United States Food and Drug Administration. The method of procedure was that outlined by Powers and Eliot in 1934. Examinations which included roentgenograms of the bones of both forearms and measurements of the weight and the length from the crown to the heel were made at monthly intervals from approximately 1 through 6½ months of age.

Of the 567 infants studied, 59 per cent were white and 41 per cent colored; 52 per cent were boys and 48 per cent girls. Two per cent of the infants showed moderate or marked rickets and 29 per cent slight or very slight rickets; the condition of 1.8 per cent was classified as doubtful, and 51 per cent remained normal throughout the period of observation. The findings must, therefore, be interpreted as referring almost exclusively to the incidence of slight or very slight rickets. The dosage level was sufficiently high to prevent the development of moderate or marked rickets except in a few cases.

In evaluating the results of the study, color, sex and the rate of growth in length were found to be important factors in the incidence of the disease. Slight rickets developed more frequently in white infants than in colored infants, regardless of the type of antirachitic administered. There was, moreover, a tendency for the disease to develop more often in boys than in girls. In this connection

it was of interest to find that colored infants grew more rapidly than white infants, that in each color group the boys grew more rapidly than the girls and that within each of the color and sex groups the more rapidly growing infant was the one more likely to show rickets.

The results indicate that:

1. There is definite evidence that evaporated milks containing about 400 U. S. P. units of vitamin D per reconstituted quart are more effective in the prevention of rickets than cod liver oil administered at approximately the same dosage level.

2. There is no evidence that cod liver oil as a preventive is superior to viosterol, unit for unit.

3. There is no definite evidence that one type of milk at the 400 unit level is superior to another in the prevention of rickets.

4. Within the dosage range used for each type of antirachitic substance the higher levels appear to be more effective, provided the basic factors of color and sex are taken into consideration.

5. Advance from very slight to slight rickets or from slight to moderate or marked rickets was found to have occurred in 24 of 112 infants observed from 1 to 6 or more months of age. It tended to occur more frequently in infants who received cod liver oil than in those who received the other types of antirachitic agents, and the dose administered was less than 750 units in all the cases. Moreover, of the 10 infants in the total group studied who showed an advance to moderate or marked rickets, 7 had received cod liver oil (in no case when the daily average number of units was more than 750); 3 had received vitamin D milk at the lower dosage level, and none had received viosterol.

6. Complete healing of the slight rickets discussed occurred more promptly among infants who received evaporated milk at the 400 unit level than among infants who received any other form of vitamin D at this level. Of the different types of vitamin D milk containing 400 units, that to which viosterol was added appeared to be the most effective. This form also tended to be more efficient than viosterol alone, even when the latter was given at a somewhat higher dosage level. When given at a dosage level of approximately 675 units, viosterol tended to bring about complete healing of slight rickets more promptly than cod liver oil given at the same dosage level.

7. When the dosage level is relatively high (over 400 units), the incidence of slight rickets has been shown to be closely and consistently related to growth in length, whereas for infants in the group who received the lower dosage there is no consistent difference in the incidence of rickets. This would indicate that at the higher dosage level the balance between rickets-producing and rickets-preventing factors has been stabilized to such an extent as to allow the influence of rate of growth in length to become evident. On the other hand, when a smaller amount is given the effect of growth in length is lost in the influence of the stronger influence of an inadequate amount of vitamin D.

8. It appears from these findings that if rickets is to be prevented or promptly controlled an amount of vitamin D must be given that will assure stability in the metabolic processes providing for normal growth of bone and allow an adequate margin of safety for the rapidly growing infant. From the data here presented this amount would appear to be at least as high as that contained in the usual dose of cod liver oil, namely, 2 or 3 teaspoonfuls.

Finally, in evaluating the results of such a study, it should be borne in mind from the point of view of public health as well as from that of the individual infant that the value of a substance containing vitamin D should be measured first in terms of success in the prevention of rickets under practical conditions and second in terms of economy. Such economic considerations must include not only the cost of the vitamin but also the need and cost of other nutrients supplied by the substance containing vitamin D.

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VITAMIN D. MILK. DR. P. C. JEANS and GENEVIEVE STEARNS, PH.D. (by invitation), Iowa City.

For the past seven years we have studied by means of balance experiments the retention of calcium and phosphorus by babies fed a constant type of diet but with varying amounts and sources of vitamin D. Most of the observations have been with cod liver oil, cod liver oil concentrate milk and irradiated milk. From these it has been concluded that the vitamin D of irradiated milk and of cod liver oil are of the same value, unit for unit, irrespective of the dispersion of the vitamin D of cod liver oil in milk. It appeared also that retentions with 1 teaspoonful of cod liver oil (350 U. S. P. units) or with milk containing 400 units equaled the maximum retentions to be obtained on a physiologic basis.

The linear growth of infants corresponded to the average curves for growth of Stuart and of Kornfeld when milk containing 135 units was fed. With the feeding of milk containing 400 units or of 1 teaspoonful of cod liver oil the rate of growth exceeded these averages. It is believed that the greater rate of growth observed with 1 teaspoonful of cod liver oil is more nearly a normal rate than the average rates which have been published.

If irradiated or other milk containing 135 units does not permit optimum retention of calcium and phosphorus and optimum growth, this amount of vitamin D should be considered inadequate, despite the fact that it usually prevents rickets. The prevention of rickets alone cannot be accepted as a criterion of adequacy of vitamin D.

During the past winter retentions have been observed in babies receiving yeast milk with a level of 135 U. S. P. units of vitamin D to the quart in comparison with irradiated milk containing the same number of units. No significant difference in retentions was observed, and the curves for growth of the two groups were of the same range. This is interpreted to indicate that the two varieties of vitamin D are of equal potency.

During the past winter viosterol in oil has been fed in comparison with viosterol homogenized in milk at a level of intake of approximately 50 units per kilogram of body weight. This level of intake corresponds to that which is obtained with milk containing 400 units. From the results it appears that viosterol in oil has the same potency as viosterol in milk. Though viosterol milk was less potent than irradiated milk, it appeared to be much more than half as potent.

The results of the studies of yeast milk and viosterol milk may not be significant because of the relatively small number of observations. The data of the other studies discussed are believed to be of sufficient quantity to be statistically significant.

DISCUSSION OF PAPERS READ BY DR. DRAKE, DR. ELIOT AND DR. JEANS

DR. F. F. TISDALL, Toronto, Canada: So much information has been given in these three papers that I must admit that I am in a daze. It is interesting to note that Dr. Eliot had no controls. Knowing Dr. Eliot's official position at Washington, it is evident that it would be impossible for her to have controls, that is, babies who did not receive any vitamin D.

Fortunately for us in Toronto, Dr. Drake was able to observe 244 babies who received no vitamin D. Among these 244 babies, 50 per cent did not show rickets, which is exactly the same figure that Dr. Eliot reports for her series of babies who received some vitamin D. This difference may be explained probably on two different bases. First, Dr. Drake's subjects, I think, were a little older than those of Dr. Eliot; and, second, what is probably more important, all Dr. Drake's subjects were of northern European descent, no colored infants being observed.

Dr. Drake brought out that in the case of infants under 6 months of age, if one does not give vitamin D 1 in 8 will show a degree of rickets of great concern to the pediatrician.

It is also of interest to note the tremendous difference between the effect of a diet containing no vitamin D and the effect of a diet containing an amount as low as $\frac{1}{10}$ teaspoonful of cod liver oil. Dr. Drake found that with this extremely small daily amount not a single infant showed severe or moderate rickets.

DR. THOMAS B. COOLEY, Detroit: I might furnish a few controls in place of those which Dr. Tisdall mentioned that Dr. Eliot lacked.

My associates and I happened to have a series of infants collected in much the same way as Dr. Eliot's, which accidentally serve as controls for her series because they did not receive the food that we supposed they were getting. We were using them for another purpose, and they were intended to have irradiated evaporated milk for their standard diet, but through some mistake the milk company sent a supply which had not been irradiated, so that between the ages of approximately 6 and 21 weeks the babies had no vitamin D. Dr. Eliot read the x-ray films taken at the end of this period, and her findings as to the incidence of rickets showed that 28 per cent of the infants were normal, 38 per cent had slight rickets, 28 per cent had moderate rickets, and 8 per cent had severe rickets.

We have been interested in the variations in various persons' reading of x-ray films for rickets. This is a matter of some importance, as this is a method used in biologic assay. I have figures on the readings of a set of films by Dr. Eliot, Dr. Jeans and Dr. Gilles and 3 pediatricians and 2 roentgenologists of our own staff. The differences are marked in some cases, though chiefly in regard to the very slight indication. I have not time to read all these figures, but shall give the readings of Dr. Jeans and Dr. Gilles as compared with those of Dr. Eliot. The comparison is not exact, as Dr. Eliot read a somewhat larger number of the films than Dr. Jeans and Dr. Gilles.

TABLE 1.—*Comparison of Readings of* X-*Ray Films*

	Jeans and Gilles, Percentage	Eliot, Percentage
Normal	40.5	52.7
Slight rickets	33.6	0.6
Slight rickets with healing	6.0	16.6
Moderate rickets	9.5	2.6
Moderate rickets with healing	1.7	12.6
Active rickets	3.5	2.6
Doubtful	4.3	12.0
Healed rickets	0.9	....

DR. A. A. WEECH, New York: I should like to remind this audience that the point of view regarding the prevention of rickets may differ depending on whether one faces the problem from the standpoint of the public health officer or from the standpoint of the clinician. Public health measures must be directed toward the goal of reducing the percentage incidence of rickets to a minimum, and this goal must be reached in a practical way. The clinician often feels that he cannot afford to have any cases of rickets in his patients; he is not sure that mild rickets should be regarded as a physiologic manifestation of growth, and he would like to eliminate it, too. This circumstance probably accounts for the unwillingness of many physicians to restrict antirachitic measures to the lower levels of dosage furnished even by the more potent vitamin D milks. Although it is disturbing to note that increasing the dose of vitamin D does not materially lessen the incidence of mild rickets, it is worth while to remember that this goal of complete protection has been realized in a natural way. I think, Dr. Eliot, that I recall correctly that the group of 500 or more babies studied by you in Puerto Rico failed almost entirely to exhibit roentgenographic evidence of mild rickets. I should like to know why the administration of vitamin D by mouth, even in high dosage, does not afford the same protection against mild rickets which is attained when babies live naked in the sunlight. Although I am willing to agree that rickets which does not reach the moderate or severe stage is probably unimportant clinically, I should like to ask whether evidence has been assembled to support this impression.

DR. BENJAMIN KRAMER, Brooklyn: Several years ago Dr. Gittleman and I carried out a preliminary study of the relative curative value of two vitamin D milks, namely, irradiated milk and yeast milk. We were unable, in this particular study, to demonstrate any difference, unit for unit, between these two milks.

During the same period we carried out a number of balance studies on some of the children. Some of the subjects received 1 quart (946.4 cc.) of milk daily containing 110 units of vitamin D, while others ingested 160 units in the form of irradiated vitamin D milk.

To our surprise, we found that the retention of calcium and phosphorus per day was about the same with both doses and compared well with the amount retained in the experiments with ultraviolet irradiation reported by Holt and his co-workers.

Furthermore, it seemed that 105 U. S. P. units did not represent the minimal dosage capable of definitely affecting the retention of calcium and phosphorus.

It was also interesting to note that the effect of vitamin D on the retention of calcium and phosphorus was demonstrable within four days after the administration of the vitamin and before we could obtain any significant change in the concentration of the calcium and phosphorus of the blood serum.

DR. HENRY J. GERSTENBERGER, Cleveland: I listened with a great deal of satisfaction to the evidence that small doses of cod liver oil are adequate for the prevention and cure of rickets, a theme about which I have spoken many times in the last years.

A few years ago when my associates and I were doing work similar to that done by Dr. Kramer, checking yeast milk and irradiated milk, we found that they were identical in antirachitic value, but we did not at that time have the opportunity to check the antirachitic value of cod liver oil. We did that in the past year to a certain degree. We studied 8 infants and found that 40 Steenbock units (180 U. S. P. units) cures rickets when given as pure cod liver oil once daily.

DR. JOSEPH J. STOKES JR., Philadelphia: I should like to mention two studies which were conducted at the Children's Hospital and the Hospital of the University of Pennsylvania throughout the past winter. At the University Hospital approximately one half of a group of 107 infants received 5 drops (0.3 cc.) of percomorph liver oil, and the other half received 10 drops (0.6 cc.). This represented a little more than 1,000 units of vitamin D and a little more than 2,000 units of vitamin D, respectively. At the Children's Hospital another group of 113 infants, also within the range in age that Dr. Eliot mentioned, from 1 to 6 months, received irradiated evaporated milk.

Among the group of 113 who received irradiated evaporated milk, with approximately 135 U. S. P. units of vitamin D per quart, there were 6 deaths due to accidents at home or to an intercurrent infection.

Among the 107 infants who remained, 11 had moderate rickets at the beginning of the study, with healing in all cases in from six to fourteen weeks. Eighty-one showed no evidence of rickets at any time; at the end of the study 14 showed signs interpreted as those of very mild healed rickets, and 1 showed very mild rickets during the study, with healing in twenty weeks at the end of the study. The growth and developmental performance of the infant were normal.

My associates and I had the opportunity to examine the ribs of 3 of the infants who died. These infants had been on milk for approximately from 2½ to 3 months of age. The three ribs examined by the roentgen rays following excision showed no evidence of rickets but when examined histologically there was evidence of very mild rickets, which was not detectable by the roentgen rays.

In connection with the roentgen diagnosis of rickets, three years ago my associates and I observed 12 colored male infants, in whom a very mild type of rickets was permitted to develop, with the purpose of placing them immediately on irradiated evaporated milk for healing. We followed them directly by roentgenograms until a rachitic condition developed.

In every one of the 12 infants we were able to determine the increasing development of rickets by means of the roentgen rays. When we showed these roentgenograms to Dr. Eliot, despite the fact that the same plates were shown several times in differing sequence, no difficulty or confusion was noted in the diagnosis.

Owing to the fact that Dr. Eliot has had a great deal of experience with the roentgen diagnosis of rickets in various clinics in the country, her observations

concerning roentgenograms have been more or less a base line for many of the studies recorded today. In the confusion that has been raised by some concerning the criteria for the value of antirachitic agents it is essential that such a base line should be accepted and understood.

In this connection Dr. Jeans has mentioned the rate of growth. My associates and I found no difference in the rate of growth and development of the groups of infants studied during the past winter, whether they received 135, 1,000 or 2,000 units of vitamin D. I have charts which I would like to show to any one who wishes to see them, in which we have compared the growth of these groups of infants.

It is our belief that had Dr. Jeans used larger groups of infants for such studies of growth and development the differences that he mentioned might not have been apparent.

DR. A. GRAEME MITCHELL, Cincinnati: This seems to be a testimonial meeting in honor of Dr. Eliot. I should state, therefore, that even in Cincinnati she has helped with a study in which Dr. Greenebaum and several others were associated. While this related to ultraviolet irradiation, it is of interest in this study since it demonstrated the small amount of therapy needed to prevent rickets.

Briefly, in a large series of colored infants it was found that none showed moderate or marked rickets provided that they received as much as eleven minutes a month of treatment with a quartz mercury vapor lamp. The criteria employed in addition to clinical observations were roentgenographic observations and, in many cases, the calcium and phosphorus contents of the blood.

DR. J. M. LEWIS, New York (by invitation): I thank the chairman for the privilege of participating in the discussion of these interesting papers.

I hope that I shall not add further to the confusion that seems to exist in regard to the question as to whether there is any distinction among antirachitic agents from the point of view of the number of rat units required to prevent or cure infantile rickets. During the past winter I have carried out a clinical investigation comparing the relative effectiveness of viosterol, percomorph liver oil, cod liver oil and irradiated cholesterol. At the beginning of the winter 441 young infants were divided into groups receiving 135 and 435 U. S. P. units of vitamin D daily in the aforementioned antirachitic agents. In addition one group of infants received 870 units in percomorph liver oil, and another group of 21 infants served as controls. Roentgenograms of the wrists of these infants were taken at the end of March and during April to determine the incidence of rickets among the various groups.

The results of the prophylactic study revealed that the degree of protection afforded by these agents at the levels mentioned was high, and that no difference in effectiveness could be noted among these antirachitics.

A curative test was also carried out and involved 15 rachitic Negro infants. Two infants received 435 U. S. P. units of vitamin D in viosterol daily; 4 received 435 U. S. P. units in percomorph liver oil; 3 received 435 U. S. P. units in irradiated cholesterol; 2 were given 435 units in cod liver oil, and 4 served as controls. Roentgenograms were taken at the end of four weeks, eight weeks, ten weeks and twelve weeks in order to determine the degree of healing. No healing was noted in the 2 infants who received viosterol for eight weeks, and at the end of ten weeks 1 infant showed slight healing. On the other hand, of the 9 infants who received either cod liver oil, percomorph liver oil or irradiated cholesterol, 8 showed definite healing and questionable healing at the end of four weeks; after eight weeks the roentgenograms revealed either marked healing or healed rickets. In the 4 infants who served as controls no healing was noted after from eight to ten weeks; 1 showed slight healing at the end of twelve weeks.

As a result of this study I am of the opinion that, unit for unit, cod liver oil, percomorph liver oil and irradiated cholesterol are more effective antirachitic agents than viosterol. It may be stated that the antirachitic factor in cod liver oil and in percomorph liver oil is probably irradiated cholesterol or an isomer of this sterol, so that it is understandable why these agents are effective to the same degree as is

irradiated cholesterol. It is interesting that a distinction among these antirachitics was brought out in the curative tests but not in the prophylactic experiments. It is possible that had lower levels of vitamin D been used in the preventive test a difference in effectiveness among these agents would have been manifest.

DR. T. G. H. DRAKE, Toronto, Canada: I just received a note from Dr. Tisdall asking me to say something about "viosterol A." Apparently he wrote this while Dr. Cooley was explaining about the strange manner in which the milk company provided nonirradiated milk for their controls. A similar incident happened in Toronto. Some one took plain corn oil and labeled it "viosterol A" and did not tell me that this meant "viosterol absent." May I say that my associates and I could get some high grade testimonials as to how well these infants did on "viosterol A."

I wish it to be noted that in my paper I thanked Dr. Eliot for reading the roentgenograms. When my associates and I started the observation we wished to be absolutely certain that the best was done in every possible way. In Toronto we believe that Dr. Eliot's reading of roentgenograms is the best that can be obtained. In visiting various clinics in the country we found that the same value was placed on her reading. Hence, we bothered her considerably and hope that if we do further experiments we shall be able to obtain the same high grade reading of roentgenograms which we believe is without a peer anywhere in the country.

DR. MARTHA M. ELIOT, Washington, D. C.: Dr. Tisdall spoke of some of the reasons why the incidence of rickets may vary under different circumstances, such as the differences in race and age in the groups of infants studied by Dr. Drake in Toronto and in the groups that my associates and I have observed in Detroit. One of the reasons for the increased incidence among the infants observed in Detroit is the frequency of observation during the early months of life. If roentgen examinations are made five or six times during the first 5 or 6 months of life instead of three times, certain changes may be found which will be missed if the observations are less frequent.

I am glad that Dr. Cooley reported the results of the roentgen readings made by a number of different observers on the "control" group of infants that he followed with Dr. Macy in Detroit two winters ago. Though there appeared to be considerable disagreement in some cases, it is evident that the agreement with respect to moderate and marked rickets was close and, in the case of mild rickets, even closer than I would have supposed it to be.

The question has been raised as to the relationship between mild rickets and growth. It has sometimes been suggested that the bony changes seen in the x-ray films and diagnosed as signs of slight rickets are merely signs of rapid growth. It is our belief, however, that these changes are not simply manifestations of rapid growth but are evidence of a mild degree or an early stage of rickets developing in a rapidly growing infant.

I was interested in Dr. Weech's remarks on the difference between the aim of the clinician and the aim of the public health officer with respect to the control of rickets. I think in general that what he says may be true. However, as a clinician and also as a public health worker, I believe that effort should be directed toward the complete control of rickets and that one should not be satisfied with less.

DR. P. C. JEANS, Iowa City: The whole subject of vitamin D in relation to the different sources and different dosages is most confusing. I have spent a great deal of time in the last two years reviewing and critically evaluating the literature and know to my sorrow how confusing it is.

There is no satisfactory method at present of getting all the controversial views together into harmonious agreement. The controversy is destined to continue until more work is done. If one goes through the literature critically certain errors in evaluation can be found. In trying to arrive at some conclusion a critical view is essential.

It has been stated today in one of the presentations that irradiated milk and viosterol are equivalent, or nearly so, unit for unit. The lowest level at which viosterol has been fed in a recorded experiment is in amounts supplying 270 units

of vitamin D a day. This has been effective in preventing rickets. The low level of vitamin D in feeding irradiated milk has been from 60 to 90 units daily. This also has been effective in preventing rickets. On the basis of such experimental data the conclusion that these two varieties of vitamin D are approximately equivalent in potency is scarcely valid.

May I add my testimonial to those which have been given in regard to the work of Dr. Eliot in reading x-ray films? She has been kind in assisting my associates and me also. The difference between us represents a difference in point of view. My associates and I believe that if maximum physiologic retentions of calcium and phosphorus are obtained continuously over a long period what appears in the bone roentgenograms cannot be signs of rickets. The changes in dispute are so slight that Dr. Drake and Dr. Tisdall have stated they have no clinical significance. If these changes occur at the same time that maximum retention of calcium and phosphorus is observed I think that one may at least question the clinical significance as well as the diagnosis of rickets. The discrepancies which Dr. Cooley reported concern chiefly differences in bone structure so slight that the interpretation has been a cause of perplexity.

Again I wish to add my tribute to Dr. Eliot's ability to read x-ray films and to repeat the reading with the same result.

AMYOTONIA CONGENITA WITH REPORT OF HISTOLOGIC STUDIES. DR. AUBREY K. GEDDES, DR. W. H. CHASE (by invitation) and DR. W. V. CONE (by invitation), Montreal, Canada.

Two patients who showed the classic clinical picture of amyotonia congenita were studied at necropsy. The cases are reported because the histologic changes put them in an intermediate group between true amyotonia congenita (Oppenheim's disease) and a similar condition that develops in early childhood (Werdnig-Hoffmann's disease).

Most of the reported cases indicate that in typical amyotonia congenita the pathologic lesion occurs during intra-uterine life. The remaining anterior horn cells do not continue to degenerate after birth, and the muscular changes do not progress. In these two cases, however, there was evidence of: (1) progressive degeneration of the anterior horn cells, (2) glial scarring in areas of loss of anterior horn cells and (3) fatty degeneration of voluntary muscle.

A further observation, which we are not prepared as yet to evaluate, is the presence of nerve cells in the white matter of the spinal cord, anterior to the ventral horn, and in the anterior roots. Many of these atopic ganglion cells showed axonal chromatolysis.

Our cases suggest that a developmental defect may be prerequisite to the disease. The cause of the progressive degeneration, however, remains obscure.

The skeletal muscles are symmetrically small, but their arrangement is unaltered. Many individual fibers are embryonic, and many show fatty degeneration. In respect to the progressive degeneration of anterior horn cells, the fatty degeneration of muscle and the advancing clinical symptomatology, the condition suggests Werdnig-Hoffmann's disease, in which anterior horn cells are progressively destroyed and degeneration of muscle is secondary to the nerve lesion.

Second Session

Thursday Evening, June 11

INFANT MORTALITY IN A MATERNITY HOSPITAL. DR. WALTER L. CARR, New York.

Read by title.

ALLERGIC TUBERCULOUS PURPURA. DR. H. P. WRIGHT and DR. H. L. BACAL (by invitation), Montreal, Canada.

The literature on allergic tuberculous purpura is reviewed and the following case reported.

R. B., a boy aged 13 years, was brought to the outpatient department of the Children's Memorial Hospital on May 7, 1934, for a check-up, because his father had died of pulmonary tuberculosis three and one-half months previously. Physical examination by Dr. H. L. Bacal gave essentially negative results. A test made with 0.1 mg. of old tuberculin injected intradermally was markedly positive in forty-eight hours. Generalized purpura (petechiae) appeared seventy-two hours after the old tuberculin was injected, and the patient was therefore admitted to the hospital. Roentgenograms of the chest were negative. For four days the patient had a slightly elevated temperature, the highest reading being 102 F. The temperature then became normal, and the rash faded.

Examination of the blood showed: hemoglobin, 82 per cent (Hellige); red blood cells, 4,820,000; white cells, 3,550; reticulocytes, 0.7 per cent; platelets, 170,000; clotting time, three and one-half minutes (capillary tube); clot reaction, normal; bleeding time, two and one-fourth minutes (Duke). The differential count was as follows: polymorphonuclear leukocytes, 56 per cent; lymphocytes, 7 per cent; mononuclears, 15 per cent; eosinophils, 12 per cent; basophils, 1 per cent; basket cells, 9 per cent. On the patient's discharge from the hospital three weeks later the white cell count had risen to 8,600, and the number of eosinophils was reduced to 1 per cent.

The results of the tuberculin tests (intradermal) with no recurrence of purpura were: on May 26, with 0.001 mg. of old tuberculin, 0; on May 30, with 0.01 mg. of old tuberculin, — —; on June 3, with 0.1 mg. of old tuberculin, — — —.

Patch tests with phenol and glycerin were negative. Skin tests made by the scratch method with fifty possible antigens prepared by Dr. Bacal were all negative.

When the patient was tested with 1 mg. of old tuberculin on readmission in June 1935 purpura recurred.

VALUE OF ECCENTRIC AND LATERAL ROENTGENOGRAMS OF THE CHEST. DR. CHARLES HENDEE SMITH, New York.

The usual roentgenogram of the chest taken in the anteroposterior direction obviously gives a projection on the film of two dimensions only. No information is given about the third. If stereoscopic films are perfectly taken, depth is suggested but not always adequately. The lateral view gives better information of the situation, size and shape of many abnormal shadows. For example, thin diffuse shadows in the roentgenogram taken in the anteroposterior position are often found to be plaquelike areas of consolidation along the interlobar fissures. Indeed, in nearly all cases lobar pneumonia seems to begin along the great fissure. Interlobar affusion can be visualized only by lateral views. Shadows at the center or toward the base of the pulmonic field may be cast by pathologic changes in the upper, lower or middle lobe. A lateral view will determine which lobe is involved. This is of importance in many conditions but especially so in fibrosis associated with bronchiectasis. Calcified shadows in the hilar region in the anteroposterior view may be in front of or behind the root of the lung, and represent a parenchymal lesion, not a calcified lymph node. Pleural effusion at the extreme base of the lung is often masked by the diaphragm in the anteroposterior view but may show in the lateral view. A lateral view of the chest of every patient has been taken as a routine in the Children's Medical Service of the Bellevue Hospital for several years. This has cleared many obscure diagnoses and added much to the modern concepts of pathologic changes in the lungs.

Lesions in the lower lobe of the left lung are often concealed by the shadow of the heart in the usual film. Oblique views do not always bring out the retrocardiac region, since the vertebral column and the heart cover most of the left

pulmonic field. To avoid this difficulty an original position was worked out more than ten years ago with the aid of Dr. Irving Schwartz. This has been used for all patients who show signs in the lower part of the chest on the left and also for those patients who are believed to have pneumonia but who have no physical signs. The technic is simple. The patient lies flat on his back with the film beneath him. The tube is placed at a distance of 3 feet (91.4 cm.), but is moved 18 inches (45.7 cm.) to be left of the midline of the patient. In most cases this will throw the shadow of the heart just far enough to the right to bring the apex opposite the shadow of the vertebral spines. This gives the maximum view of the left pulmonic field and shows practically the entire retrocardiac region. The right side is distorted but may be ignored. This "eccentric" position has been useful in many cases of lesions of the left lung.

MEDIASTINAL LYMPHOSARCOMA IN CHILDREN. DR. ALTON GOLDBLOOM and DR. F. W. WIGLESWORTH (by invitation), Montreal, Canada.

This paper is based on a series of four cases observed in the Children's Memorial Hospital of Montreal between 1932 and 1936. The diagnosis was made by clinical, roentgenologic and pathologic examination.

The first patient was a girl aged 4 years with bronchiectasis due to lymphosarcoma of the mediastinal lymph glands. Autopsy was performed. The second patient was a girl aged 6 years with a condition that was probably lymphosarcoma of the thymus. No autopsy was performed. The third patient was a girl aged 11 years with lymphosarcoma of the thymus and leukemic changes of the blood. Autopsy was performed. The fourth patient was a boy aged 6 years with early lymphosarcoma of the thymus, without changes in the blood. Autopsy was performed.

The early symptoms are vague and uncertain, while respiratory symptoms are a late manifestation. The local and roentgenologic findings in the lungs depend on the extent of the mediastinal enlargement and the involvement of the pleura and pericardium.

The common tumor of the mediastinum in childhood is lymphosarcoma, which usually arises from the thymus. Distant metastases are not a feature of the disease, but in many cases there is a terminal leukemic blood picture. Although this neoplasm is uncommon, it is a definite clinical and pathologic entity. Treatment is purely palliative.

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MESENTERIC CYSTS IN CHILDREN. DR. I. H. ERB, Toronto, Canada.

Under the general title of mesenteric cysts a series of 10 cases of developmental cysts of the abdomen in children and, because of its similarity in manner of development, an eleventh case of cyst of the mediastinum are reported. Two of these cysts are classified as being of lymphogenous origin and were comparable in structure and development to cystic hygromas. The remaining 9 are described as being of enterogenous origin. The development of the cysts of the latter group from small diverticula or sequestrated nests of cells of intestinal or gastric mucosa is described in some detail. The series is subdivided according to the classification in table 2.

This wide variation in relation to both the wall and a segment of the gastrointestinal tract explains the varied symptomatology and the difficulties of accurate preoperative diagnosis. Various complications included intestinal obstruction, hemorrhage into the cyst and intussusception. Of the 10 patients with cysts in the abdominal cavity, all were operated on; 8 recovered. One patient, a 6 year old girl who had been ill for six days with symptoms of intestinal obstruction prior to admission, died within three hours after the operation of toxemia and shock. A 5 week old boy died of postoperative pulmonary embolus.

TABLE 2.—*Classification of Mesenteric Cysts*

I. Relation of Cysts to the Wall of the Gastro-Intestinal Tract	
Arising in the omphalo-enteric duct	1
Mural or intramural (in relation to the wall of the intestine)	5
Omental	1
Mesenteric proper	3
Mediastinal	1
	11
II. Relation of Cysts to the Segment of the Gastro-Intestinal Tract from Which They Appear to Have Arisen	
Esophagus	1
Stomach	1
Pylorus	1
Jejunum	1
Ileum (including one cyst from the omphalo-enteric duct)	6
Ileocecal region	1
	11

THE PEDIATRICIAN'S RELATION TO MENTAL HYGIENE. DR. C. A. ALDRICH, Winnetka, Ill., and DR. BORDEN S. VEEDER, St. Louis.

The authors present a topical list of the subjects that they feel fall within the pediatrician's field in mental hygiene. The topics are grouped under three main headings: (1) predominantly physical factors with psychologic effects, (2) predominantly psychologic factors with physical effects and (3) environmental factors modifying development. The importance of prevention as the field of the pediatrician is stressed because of his unique relation to the child and family. A few of the subtopics are briefly discussed by way of illustration:

Predominantly Physical Factors with Psychologic Effects.

A. Habit Formation. In most cases a transfer of subcortical reflex to cortical control. The optimum age for training must be considered in each case.

1. Appetite
2. Sleep
3. Bowel and bladder control
4. Physical skills
5. Play
6. Personal hygiene

B. Associations with Ill Children. Bedside technic, pain, fear of the physician, suggestion, etc.

1. Treatment of disease
2. Physical handicaps
3. Fatigue

C. Mental Subnormalities on a Physical Basis. Possibilities for care at home and in schools.

1. Mongolism, cretinism, microcephaly, etc.
2. Injuries to the brain, hemorrhage, trauma, inflammation, etc.

D. Functional Disturbances on a Physical Basis. Educational opportunities and the physician's advice.

1. Reading and speech difficulties due to mixed cerebral dominance

Predominantly Psychologic Factors with Physical Effects.

A. Emotions. Those important in the formation of habits and the development of personality.

1. Fear
2. Love
3. Anger
4. Hate
5. Sorrow

B. Conventionally Unacceptable Habits. The physician's opportunity in prevention and early treatment.

1. Lying
2. Stealing
3. Masturbation
4. Thumb-sucking
5. Stammering
6. Nail-biting
7. Tics
8. Disturbance of sleep
9. Day dreaming
10. Heterosexual activities
11. Disorderliness and uncleanliness
12. Temper tantrums

C. Relations to Society. From birth the physician must understand the complexity of the child's problem.

1. Negativism
2. Pathologic attachment to mother or nurse
3. Antisocial behavior

D. Intellectual Attainment. The physician must be able to give an approximate opinion.

1. Precocity
2. Mental retardation

E. Motor States. The physician must recognize types in order to fit the patient into his environment.

1. Hypermotility
2. Hypomotility

F. Adolescence. Understanding of the major psychologic processes at this time.

Environmental Factors Modifying Development.

A. Education. Of major importance in physical development and the development of personality.

1. Parent
2. Nurse or nursemaid
3. Physician
4. Child's school

B. Relation to Other Children in the Family. May be the cause of abnormal behavior in children.

C. Playmates.

D. Socio-Economic Factors. Perhaps the most important modern consideration in physical and mental health.

DISCUSSION

DR. HERBERT B. WILCOX, New York: One point in connection with what has been said will bear emphasis. That is the preventive opportunity offered to the pediatrician in the matter of mental health of the child.

Last year it was said before this society: "The notion that pediatricians are dealing with incipient mental disease and preventing 50 per cent of it dooms us to frustration."

How would this sound if applied to the recognition and management of rickets? The opportunity for prophylaxis is fairly comparable in these two conditions, and on this fact depends the importance of the acceptance by every children's physician of direct responsibility for his patients' mental health or temperamental content.

In the earlier years of this organization infant feeding furnished the greatest stimulus for discussion. More recently rickets has assumed this rôle. It is fair to prophesy that the coming years will see the matter of mental hygiene in infancy and childhood replacing both these subjects.

It is rather curious that the problem of infant behavior—the proper management of difficult children and the deviations from the normal in these respects during the early years—should have been so long in assuming a prominent place in the thought and activity of the pediatrician. To be sure, the question comes in somewhat unaccustomed garb. One cannot estimate its p_H. One cannot put it in a test tube and subject it to chemical analysis. But, nevertheless, these behavior problems may be accurately analyzed and evaluated to the end that therapy may be intelligent and effective. It should be as important to the pediatrician as is his recognition of any organic or functional disturbance.

The frequent occurrence of these difficulties makes them of daily practical importance.

If it is true that, in the school, this sort of problem occurs in from 3 to 5 per cent of children, many a teacher may find the cause of fatigue here rather than in the effort of teaching the three R's.

If it is true that 50 per cent of the patients brought to the pediatrician's office come at least in part because of problems related to behavior, this problem is an important part of the pediatrician's obligation, and it becomes imperative that he should fit himself to attack it intelligently, not simply using "a psychiatric method or nomenclature," the danger of which has been emphasized.

If it is true that the incidence of behavior difficulties in patients brought to the free clinics has risen from 2 or 3 per cent of a few years ago to from 10 to 15 per cent it becomes the duty of the dispensary physician to interest himself in helping the tired mother to control her children better and to give advice not only as to digestion or disease but also as to their general behavior.

If one considers the etiologic factors which may play a part in bringing about behavioristic troubles in children, one gets a lead of definite therapeutic value. There are various approaches to their appreciation and management.

In regard to the organic theory, it has been said that 50 per cent of difficult children are so because they are physically uncomfortable. In many instances the condition is explainable, perhaps, on the physiologic theory.

The endocrine glands may play a contributory part, particularly in those problems arising during the period of puberty, but much of this theory has proved unfactual and not free from danger.

The additional approach to the problem which I would emphasize and which bids fair to be more comprehensive, is the pediatric approach. The pediatrician must be allowed to "interpret behavior as well as judge conduct" if he is to advise as to control. There is no reason why the pediatrician should not be thoroughly equipped to give such advice. As has already been said, he gets his opportunity earlier than either the psychiatrist or the educator. The pediatrican is there (if the obstetrician will allow) while the child is a *potential* problem.

One might fairly distribute the responsibility for this phase of psychiatric work by allotting the potential parent to the psychiatrist directly but reserving the actual parent for the pediatrician, who can best gain cooperation through parental interest in the child.

Bakwin has well defined constitutional make-up as the result of the impact of environment on inherited material. Hereditary influence is vastly complex, involving many generations, and is entirely beyond modification or control.

The physical and temperamental environment, however, is tangible, capable of being met intelligently, definitely modified, perhaps corrected and deprived of its detrimental characteristic if the pediatrician on the spot realizes his responsibility in this respect and is equipped and eager, as he should be, to do something more for his patients than supervise normal growth and development or treat organic disease. Perhaps the pediatrician who fails to recognize this important part of his work is as guilty therapeutically as the nagging parent is etiologically, of whom Emerson said: "Respect your child. Be not too much his parent. Intrude not on his solitude."

HORTON R. CASPARIS, Nashville, Tenn.: Dr. Aldrich and Dr. Veeder have brought to the attention of the members an important subject. Physical health means little unless one has learned how to live with other persons. In other words, healthy behavior of a human being is just as important as a healthy body. The two together make up the whole human being and are therefore indissociable. It goes without saying, then, that the physician, who more than any one else is familiar with the human body, should assume responsibility for the health aspects of the behavior of that body, that is, the reaction of the body to its environment.

Before going further I should like to make a plea for applying the term "health" rather than "hygiene" to behavior, just as one applies the term health to physical structure and function. One is just as much a matter of health as the other, and since health is such a familiar term I believe that if one will place mental health on the same plane as physical health, and use the expression "mental health" rather than "mental hygiene" there will be a much wider acceptance of its significance.

Physicians have failed to assume this responsibility partly because medical schools have been deficient in their teaching and partly because a great deal of confusion has been created by some of the writers on the subject. One gets the impression from the literature that this is an intangible and nebulous subject, while, on the contrary, it is about as specific and definite in its preventive aspects as are many of the practices that are employed in the care of the human body. Child psychology is not a special brand of psychology but is nothing more or less than human psychology. There is no fundamental difference between a child and an adult. As one grows older and accumulates experience one learns to modify one's behavior, but the basic inclinations and desires to get and avoid are the same. One spends one's time, regardless of age, trying to get what one wants and trying to avoid what one does not want. One wants that which produces pleasure and comfort, and one does not want that which produces displeasure and discomfort. One is considered healthy mentally if one learns to face the rough side of life with reasonable equanimity just as one enjoys the smooth side of life. There are certain basic principles or laws which guide human beings toward such stability, and these basic laws are nothing more or less than common sense, which always has and always will be the foundation of adequate human conduct.

The pediatrician does not have to be a psychiatrist to take advantage of this information, and it is certainly his responsibility to do so, since it is the pediatrician especially who has the opportunity to begin at the beginning with the human being and try to build for him an adequate existence. I purposely use the term "adequate" rather than "normal" because no one knows what normal is, but all that matters is that one be adequate for life as one faces it or for the problem which confronts one.

The indications for building in any particular child courage, honesty, self-respect, reliability, ambition and so forth are definite, even though they happen to be difficult to carry out in many instances. The methods by which one keeps children from lying and stealing are also definite. What can be expected from the inheritance of any individual child is not beyond the pediatrician's ability to work out. Mental nutrition, even though it is intangible, is about as specific as physical nutrition and is equally essential. It is made up of the satisfaction of accomplishment more or less commensurate with one's ability to accomplish.

In brief, the elements which make up human behavior are specific and definite, and it is just as much the pediatrician's responsibility to supervise and direct the building of adequately behaving human beings as it is to supervise their

physical health. He is basically better prepared than any one else to assume this responsibility, and I think that the members are indebted to Dr. Aldrich and Dr. Veeder for emphasizing the importance of the pediatrician's relation to this subject.

DR. ALTON GOLDBLOOM, Montreal, Canada: I do not wish to enter deeply into this discussion or prolong it unduly, but I feel that this is an excellent opportunity to call attention to the fact that of all the welter of literature that has appeared in the last twenty-five years on mental hygiene as applied to children no work has yet appeared which is equal to a small book written nearly one hundred years ago by Herbert Spencer called "Education." It is not only a book that every pediatrician should read and know thoroughly but a book that can be recommended to every mother to read and to use as a guide in the rearing of her children. I think that many of the problems that are presented to parents and that are being discussed here tonight will be simply and adequately solved through the reading of this book, which is entirely nontechnical and has no nomenclature.

DR. B. RAYMOND HOOBLER, Grosse Pointe, Mich.: I remember about ten years ago when this society first began to realize that there were two groups of persons, perhaps professionals, coming into prominence to take part of the practice away from the pediatricians. There was considerable discussion on this subject. Those two groups of persons were the psychologists and the psychiatrists.

Pediatricians had many a long discussion as to how they were going to "head off" these persons who seemed to be "muscling in" on pediatrics. They seemed at first to take the question lightly. They were thoroughly prepared to handle all these problems themselves.

After attending a few clinics and a few demonstrations by both psychologists and psychiatrists they made up their minds that perhaps they did not know all that there was to know as "pediatrists" regarding carrying on and developing the mental state of children. So that pediatricians for a time were greatly stimulated in this study.

I remember that Dr. Veeder, in circularizing the teachers of pediatrics in this country, urged them to put in courses on behavior clinics, on various forms of psychiatry and even on psychology.

At that time, fully ten years ago, I called in one of the younger pediatricians who was attached to an institution where a great deal of psychology and psychiatry from the standpoint of infancy was being taught according to the theories of the Merrill Palmer School in Detroit. Most of the members have heard of that institution and its splendid work in psychiatry and the psychologic aspects of the training of children.

It seemed at that time that the students received a great deal of information which was helpful from the standpoint of handling that hiatus beween the purely physical pathologic ills of children and the mental ills.

I think perhaps the older pediatricians, not having had that distinctive and definite training, have been rather loath to step into that field, although as has been mentioned, splendid books have been published that can help the average pediatrician accomplish all that is necessary in handling these cases. But it requires a great deal of work and a great deal of attention to equip oneself properly to handle the work which the psychologist and the psychiatrist are doing. I think that perhaps most of the medical schools today are giving training in this line, but most of the pediatricians who graduated ten years or more before this have not had that particular training, and it requires a great deal of study to accomplish the best so that they can be true advisers to the mothers and fathers of their patients.

DR. CHARLES HENDEE SMITH, New York: I was a great admirer of the late John Ruhräh, as all the members were, I am sure. One of the crusades that he conducted was against the term "pediatrician." I have struggled hard to follow him in calling myself a pediatrist, but Dr. Hoobler is the only one who has used this term in this discussion. Would it not be a good thing to have a committee decide what we really are?

DR. C. A. ALDRICH, Winnetka, Ill.: It has been gratifying to hear this sort of discussion.

As I listened to Dr. Wilcox's reference to the importance of environment in the development of behavior it seemed to me that the pediatrician should thoughtfully consider his influence as integral parts of the environment of his patients. It is possible for him to make his section of the environment plastic and healthful so that it will fit the needs of his developing charges and aid them in their adjustments. Too rigid instructions as to routine care tend to increase rather than to decrease the problems of children.

Dr. Casparis spoke of his preference for the term "mental health" rather than "mental hygiene." I like the latter, because to me, at least, it has a preventive implication, but this is a matter of individual choice.

It should be emphasized again in this connection that there is no such thing as the purely mental or the purely physical concept in dealing with children. Factors affecting one must influence the other, and the point where the one leaves off and the other begins is not accurately definable.

We should like to point out again that our prophylactic force has not yet been sufficiently developed. We have presented the outline with the hope that it would provide something definite for consideration. If the groups who are interested could seat themselves around a table and discuss these various problems, perhaps concrete advance could be made quickly.

Third Session

Friday Morning, June 12

EVOLUTION OF THE ADULT TYPE OF TUBERCULOSIS FROM THE CHILDHOOD TYPE; EVIDENCE IN FAVOR OF ENDOGENOUS REINFECTION. DR. J. A. JOHNSTON, Detroit.

Six hundred and fifty persons from a poor economic stratum who reacted to 0.1 mg. of old tuberculin were observed for varying periods up to seven years following removal from their source of infection. Twenty-three cases of tuberculosis of the adult type were found, in 16 of which the condition developed subsequent to the initial observation. There have been only two deaths from miliary tuberculosis since the study was started, a result which is interpreted as favoring the view that something has been accomplished by this system of follow-up and care in preventoriums. No consistent relationship could be discovered between the onset of the reinfection type of tuberculosis and a quantitative change in allergy. The basal metabolism of this group was found to be approximately normal. The metabolic mixture and the retention of nitrogen suggested depletion of metabolic stores at the time of the phenomena of reinfection.

DISCUSSION

DR. FREDERIC W. SCHLUTZ, Chicago: I do not think that Dr. Johnston or any of the members need to be too disturbed about the statements made by Dr. Myers and Dr. Stewart with reference to the advantage of follow-up in preventoriums in these cases. I am sure that they did not mean to state their opinion in so dogmatic a form as it seems to be accepted.

I am familiar with the material with which they are dealing in Minnesota. This is a type of material probably entirely different from that encountered in cities like Detroit or any other large metropolitan center like Boston, New York or Chicago.

What might be a desirable requirement in that type of material would not be so necessary in the type of material encountered in a state like Minnesota with the economic conditions prevailing among the classes with which the investigators are dealing and on which their case reports and conclusions are based.

There can be no question in the minds of any of the members of the advantage of the treatment in preventoriums in the type of cases to which Dr. Johnston refers.

DR. H. P. WRIGHT, Montreal, Canada: I was much interested in the paper which has just been read. I also was at the meeting of the National Tuberculosis Association last year and also felt that the point brought out by Dr. Myers and Dr. Stewart was overemphasized.

There is no question in my mind that exogenous infection is important, but I do not think that any one who has to do with children could feel that many cases of fatality occur as a result of exogenous reinfection, considering the mortality rate and the number of reactors to old tuberculin.

In Montreal there is a great deal of tuberculosis, and forty-two beds are set aside at the Children's Memorial Hospital for patients with pulmonary tuberculosis. During the last year there were six deaths, four from miliary tuberculosis with associated meningitis and two from miliary tuberculosis without any involvement of the meninges.

I should like to present the thought as to how tuberculosis heals. I feel that the term "childhood type" as adopted by the National Tuberculosis Association is still a safer term than "primary tuberculosis," although it is obvious that in most cases of the childhood type the condition is manifestly a primary infection.

One speaks familiarly about the Ghon tubercle and the formation of calcium. I am not sure that one wishes to see evidence of calcification. Pneumonia clears without calcification, and even though Opie and others maintained that calcification always occurs in tuberculosis and sometimes is so minute that one finds no evidence of it, since it may be behind a rib or in the middle of the lung, it is just possible that those patients in whom tuberculosis clears without any demonstration of calcification may do better later in life than those who show marked calcification. After all, not a great deal is understood about calcification.

The question of immunity is interesting to me, as it is to all. I have had during the past year an apparent clinical demonstration that immunity does exist. Although my associates and I in Montreal have observed a group of children who are receiving BCG, I do not wish to discuss this question.

The legislation in Montreal, unfortunately, is not as good as that in Minneapolis. Some of the children have been forced to live in houses where there are persons with active tuberculosis who have tubercle bacilli in the sputum. Some of these children, after they recover from the initial lesion, seem for a time to live apparently healthy lives, which is difficult to explain unless one accepts the fact there must be some immunity. How long the immunity lasts I do not know, but I do not think that one should give up the idea of the older and experienced clinicians and say that immunity is not a factor in tuberculosis.

There is one more point that I should like to emphasize in regard to the childhood type of tuberculosis, in connection with the diagnostic standards and the means of making a prognosis. I feel that the sedimentation test is probably the best laboratory test at the physician's disposal from the point of view of the prognosis. I think that over a period of time curves for sedimentation will give an indication of when a child should be put to bed and rest.

As the reader of the paper emphasized, the physician must have some way of determining when an inactive infection may reassert itself, and, the sedimentation test, in my opinion, is the best means at his disposal.

DR. CHARLES HENDEE SMITH, New York: I am afraid that I must disagree with Dr. Wright as to the value of the term "tuberculosis of the childhood type." He mentioned deaths from miliary tuberculosis and intimated that the condition was not tuberculosis of the childhood type. I should class the condition as hematogenous generalization from a primary complex, certainly not as the adult type of tuberculosis.

The whole nomenclature of tuberculosis is still unsettled and has been somewhat more confused, it seems to me, by the adoption of the terms "childhood type" and "adult type."

Two years ago I had the privilege of sitting on a committee in which every group interested in tuberculosis in New York City was represented, including Dr. Schick, Dr. Park, Dr. Amberson, Dr. Grethman and others. We held dis-

cussions once or twice a week for several months during the winter. Two or three of those sessions were devoted to the evidence as to whether the adult type of tuberculosis is the result of endogenous or exogenous infection. The conclusion was that the evidence was about equally balanced, that there was no positive evidence in either direction.

I had hoped to hear something more about the mechanism of endogenous reinfection. My associates and I have been able to observe a number of cases in which the so-called Simon tubercles were evident, i. e., small shadows in the infraclavicular region in children two or three years after infection. These are the only pathologic anatomic evidence, as far as I know, of the possible mechanism by which an apical lesion of the adult type can arise from an old infection contracted in childhood. We have followed a number of patients with these small dense areas, have watched the lesions calcify and then have seen them suddenly soften and spread rapidly in adolescence or in the latter part of the first decade to form apical lesions of the adult type.

When the term "childhood type" of tuberculosis is used one never knows whether it is the primary complex (the primary focus of infection plus involvement of regional lymph nodes) that is being discussed or whether the disseminations which occurred in childhood (bronchogenic or hematogenous) are included. Certainly the tuberculosis of childhood includes these disseminations which take place in childhood, but these are not the same as the reinfection type of tuberculosis in adults.

It seems to me that the terms primary complex, dissemination and reinfection describe the main phases of tuberculosis more accurately than any others. What the mechanism of reinfection is still remains to be proved. It may well be from within in some cases and from without in others.

If I am correct, there was no pediatrician on the committee which decided this nomenclature, but the criteria for diagnosis were decided by those interested in the adult type of tuberculosis and in pathology and roentgenology.

DR. BÉLA SCHICK, New York: I am glad to see that many physicians do not accept the pessimistic attitude of Stewart and Myers. I had a lively discussion with Stewart at the time that I was chairman of the Round Table Conference on Allergy of the American Academy of Pediatrics. I expressed my opinion against that of Stewart and Myers, who teach that immunity and allergy have nothing to do with each other.

I do not believe the term "childhood type of tuberculosis" is as bad as Dr. Smith thinks. Under this term is included not only the primary complex but all the other features that belong to the so-called symptoms following the primary complex during the first years after infection. Disseminated foci may appear in both lungs, and the tubercular process may flare up in the infraclavicular region.

I have repeatedly discussed with Professor Ghon how he feels about the pathogenesis of the adult type of tuberculosis, whether it develops from an exogenous or an endogenous source. He was not able to decide the question definitely. He expressed the view that both endogenous and exogenous superinfection occur.

The statement of Stewart and Myers that puberty plays a rôle in the flare-up of the childhood type of tuberculosis, mostly on an endogenous basis, is not new. Myers and Stewart declared that one of the worst things that can happen to a human being is to be infected during childhood with tuberculosis, that the flare-up or superinfection in such a case from without or within is very dangerous and it would be better to be infected with tuberculosis later in life as an adult. I believe that the infection during childhood produces a certain resistance against superinfection. Endogenous or exogenous superinfection occurs especially at the time of puberty. More information is needed as to what enhances the activation of tuberculosis at the time of puberty. This puberty type of tuberculosis is similar to the adult type.

If the first infection with tuberculosis occurs in adult life, the adult will show the childhood type of tuberculosis. With the decrease of positive tuberculin reactors among children one may expect to see more cases of the childhood type of tuberculosis among adults.

DR. HORTON R. CASPARIS, Nashville, Tenn.: For the great majority of physicians who are concerned primarily with the practical phases of tuberculosis, it seems to me that it would be much better to spend less time and energy trying to differentiate the adult type of tuberculosis from the childhood type. In any individual case in which the patient is sick with tuberculosis it is practically impossible in most instances to differentiate between the two types of infection, and it is not particularly important to do so. One rarely knows when infection first occurs in human beings, and certainly knows little or nothing about the extent and frequency of subsequent reinfections. In other words, I feel that the physician should not try to transfer to human beings his fairly clear picture of what happens in experimental tuberculosis. For in experimental animals one knows the extent and time of first infections and of subsequent reinfections, and since this specific information which is so essential to a clear understanding of what happens is not available in human beings, it is manifestly impossible to superimpose the two pictures.

However, there is still much to learn about tuberculosis, and since any addition to the knowledge concerning the disease is valuable the members are indebted to Dr. Johnston for the information that he brings. It is through such careful studies as he has presented that the physician becomes better able to cope with tuberculosis in specific cases and in its broader implications. I recall two more or less accidental experiments which confirm his statements regarding endogenous reinfection. Following the widespread epidemic of influenza in 1918 there was a marked rise in the incidence of tuberculosis, which was caused, it is believed, by the "lighting up" of much endogenous reinfection by this widespread intercurrent infection (influenza). Also during and immediately after the war, in a certain part of Germany, where there was a marked shortage of food, resulting in much poor nutrition, the rate for tuberculosis rose rapidly and fell later as the poor nutritional condition was relieved. This, after careful study, I believe, was considered another instance in which endogenous reinfection became rampant as a result of a superimposed debilitating influence.

In regard to Dr. Johnston's remarks on the variability of tuberculin allergy, one should remember that there are two factors concerned in tuberculosis, namely, the infecting organism and the host. The infecting organisms vary tremendously in amount and in virulence, and likewise the hosts must vary greatly in the response to these infections. It is known that hosts vary greatly in their response to other infections and probably likewise vary in their response to tuberculous infections. So about all that can be said concerning any person who has tuberculosis is that at some time or other he received a sufficient number of organisms to make him sick.

Dr. Johnston has appropriately emphasized the importance of keeping in mind the danger of endogenous reinfection, since there is little doubt but that in many instances tuberculosis as a manifest disease develops in that less dramatic way.

DR. J. A. JOHNSTON, Detroit: The only reason that I brought up the question of allergy, Dr. Casparis, was the negative one of possibly adding a small amount of information to the point as to whether there is danger in inducing reactivity.

PIRQUET'S ISOLATION BED UNITS FOR NEW-BORN AND YOUNG INFANTS.

DR. BÉLA SCHICK and DR. SAMUEL KARELITZ (by invitation), New York.

The prevention of spreading infection, especially catarrhal and cutaneous infection, among new-born children and young infants is of great importance to the pediatrician.

Many hospitals for infants and small children have tried to solve this problem by installing cubicles or by building small rooms with from one to three beds. Both these procedures require much space. Pirquet advised, therefore, small

cribs isolated by glass walls, united in one unit of six beds. Two such units have been installed in the children's department of the Mount Sinai Hospital. The construction and the satisfactory results obtained with these units are described.

INTERRENAL RICKETS. DR. HENRY J. GERSTENBERGER, Cleveland.

A girl 11 years of age was observed at the Babies and Children's Hospital for seven days before death. On admission she showed dwarfism, melanosis, hirsutism, muscular weakness, and enlargement of the knees, wrists and ankles, which was due to rickets, as shown in roentgenograms and in the abnormal levels of the calcium, phosphorus and phosphatase of the blood serum (the calcium content was 9.5 mg. per hundred cubic centimeters; the phosphorus content, 3.5 mg., and the phosphatase content, 1.05 mg.). The urine showed a neutral reaction and contained albumin (3 plus) and some pus (from 30 to 40 cells). The roentgenograms of the kidneys showed the presence of numerous small and large calculi, apparently principally in the body of the kidney. There were also some calculi in the bladder. Other laboratory data determined at this time were as follows: The nonprotein nitrogen content was 36 mg. per hundred cubic centimeters, and the cholesterol content, 122 mg. After forty-eight hours extremely severe acidosis developed, the p_H reaching the low level of 6.9 and the carbon dioxide-combining power falling to 13 volumes per cent. The urine was neutral and contained acetone and albumin. At this point the nonprotein nitrogen content rose to 80 mg. per hundred cubic centimeters, then fell, with improvement, to 32 mg. Under antiacidosis therapy the picture of the severe acute acidosis disappeared; the p_H fell to 7.2 and the carbon dioxide-combining power rose to 24.4 volumes per cent. During the period of therapy the urine became alkaline; later it became neutral, when it occasionally contained a great many pus cells, and the amount of albumin varied from 1 to 2 plus. The excretion of phenolsulfonphthalein on the day before the onset of the acute acidosis was 2 per cent for the first hour and 15 per cent for the second hour, making a total of 17 per cent. On the day of the severe acidosis the icteric index was 5, and on the day before death Erb's phenomenon was more than 8 milliamperes.

At autopsy the following pathologic changes were observed: (1) severe atrophy of both adrenal glands involving essentially the cortical part, (2) melanotic pigmentation of the skin, (3) severe active rickets, (4) osteoporosis, (5) severe urolithiasis (renal and ureteral calculi composed of from 76 to 78 per cent calcium phosphate), (6) incomplete hydronephrosis and (7) mild interstitial hepatitis.

Quite as important as the positive observations are the negative: The parathyroid, the thyroid, the pituitary and the pineal glands, the ovaries and the pancreas were normal, as were also the gastro-intestinal tract, the brain and the spinal cord. The changes in the liver and in the kidney were insignificant; the latter were interpreted by the pathologists to be due to the presence of the renal calculi and not to a primary inflammatory or degenerative process.

It is concluded, therefore, on the basis of the data just given, that there was a direct relationship in this patient between the marked destruction of the cortex of the adrenal glands and the rickets. What the exact nature of this relationship was can only be surmised. Pertinent experimental data must be obtained for the substantiation of any hypothesis offered at this time. However, it would seem plausible to assume that the loss of sodium brought about by the destruction of the renal cortex was the prime factor concerned in both the development of the rickets and the development of the renal calculi.

The fact that the adrenal cortex is a lipoid structure also suggests the possibility that the rickets was due to some disturbance in the functioning of the antirachitic factor itself rather than to a disturbed phosphorus metabolism secondary to the acidosis produced by the loss of sodium.

Before the patient's admission to the Babies and Children's Hospital a diagnosis of renal rickets had been made by the family pediatrician during June 1933 and a diagnosis of a possible parathyroid tumor in June 1934. At operation, however, no parathyroid tumor could be found. The child received irregularly but more

or less constantly throughout her illness cod liver oil and other antirachitic substances, without any benefit. After death it was learned from the parents that the child liked sodium chloride and used much more of it than did the other members of the family.

RHEUMATIC INFECTION IN CHILDHOOD: OBSERVATIONS ON THE SEDIMENTATION RATE AND THE SCHILLING BLOOD COUNT. DR. R. R. STRUTHERS and DR. H. L. BACAL (by invitation), Montreal, Canada.

Previously reported work has shown that, on the basis of its effect on the sedimentation rate, rheumatic infection may be divided into three phases:

1. Acute rheumatic fever, a manifestation of rheumatic infection in which the sedimentation rate falls rapidly from a high level to a normal level following the subsidence of symptoms.

2. Chorea, a manifestation in which the sedimentation rate is constantly normal in the absence of complications.

3. Carditis, a manifestation in which the sedimentation rate falls slowly during a period of months to a normal level.

From this it was concluded that the sedimentation rate is the most delicate test of those investigated, which included observations on the body weight, the temperature, the pulse rate and the total white cell count of the blood to determine the activity of rheumatic infection in childhood.

It has also previously been shown that one of the factors concerned in the alteration of the sedimentation rate is an alteration in the albumin-globulin ratio of the protein of the blood serum. With increase in the sedimentation rate the globulin fraction rises, and the albumin fraction falls, returning to a normal ratio when the sedimentation rate becomes normal.

The present investigation concerns the relation between the shift in the Schilling blood count and the sedimentation rate in the determination of the activity of rheumatic infection in childhood. The conclusions reached are as follows:

1. In acute rheumatic fever, with cessation of activity of the infection the blood count returns to normal pari passu with the sedimentation rate, frequently even more rapidly. The shift may, however, still be slightly to the left when the total leukocyte count has returned to normal.

2. In chorea, with a constantly normal sedimentation rate there is no increase in the number of immature polymorphonuclear leukocytes, i. e., no shift to the left.

3. In carditis, there is frequently no apparent association between the sedimentation rate and the shift in the Schilling blood count in that the former may be markedly altered without a corresponding increase in the number of immature polymorphonuclear leukocytes.

From these observations it is concluded that the sedimentation rate is a more delicate test for the activity of rheumatic infection than is the shift in the Schilling blood count.

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DISCUSSION

DR. A. A. WEECH, New York: I wish to congratulate Dr. Struthers and Dr. Bacal on this additional clear evidence of the remarkable parallelism between rheumatic activity and the rate at which red cells settle. My experience and that of my associates at the Babies Hospital fully confirm their confidence in the parallel relationship. Not only does the test provide the best estimate of the subsidence of rheumatic activity, but also when tests are carried out frequently on subjects with quiescent rheumatic infection a sudden upward move in the rate presages an oncoming recrudescence of rheumatic activity.

The parallelism is so close as to lead one to suspect that the secret of the pathogenesis, if not of the etiology, of rheumatic disease itself may be revealed when the mechanism responsible for the sedimentation of red cells is better understood. There is little complete information on this point. A few facts are

known. One is that the variations in the rate are related to changes in the plasma and not to changes in the red cells themselves. The second is that the change in the plasma in rheumatism is a positive change, not a negative one; increased sedimentation of red cells does not occur because something is lacking which is present in normal serum and which prevents the red cells from settling but because some substance, apparently present in normal serum, is increased in amount and brings about a more rapid precipitation of the cells. It is further known that the substance which is increased is one which causes rouleau formation, and the red cells settle more rapidly because they are agglutinated. It is further known that the agglutinating substance is present both in the globulin and in the fibrinogen fraction of plasma. It has been shown that the addition of normal globulin or normal fibrinogen to normal serum will lead to striking rises in the rate of sedimentation of the red cells.

Here, however, the present knowledge stops. Whether the proteins themselves are offending substances when present in abnormal amounts, whether there is an added protein which appears to distribute itself between the fibrinogen and the globulin fraction only because the present methods of analysis are inadequate or whether there is some additional substance merely associated with the proteins is not known. It is possible that a forward step will have been made when there is increased knowledge concerning the site and manner of origin of the plasma proteins and that this knowledge may not only assist in an understanding of the erythrocyte sedimetation rate but also further the present insight into the nature of rheumatic activity itself.

Dr. John D. Lyttle, New York: In the discussion of the mechanism of the sedimentation rate most of the interest has been centered on the concentration of the protein fractions. It is interesting that Kendall, working in Heidelberger's laboratory, has found that the addition of minute amounts of polysaccharide of Streptococcus haemolyticus and Pneumococcus will alter the sedimentation rate. They have added dilutions of from 1:5,000,000 up to 1:2,000 (the maximum amount of polysaccharide of Streptococcus haemolyticus and Pneumococcus type III being 0.5 mg.) to normal blood and found a significant rise in the sedimentation rate. This indicates that there are other factors connected with infection besides the altered protein fractions that can cause an increased sedimentation rate of red blood cells.

Dr. Alfred P. Hart, Toronto, Canada: I should like to ask Dr. Struthers how the patients who showed the nodules progressed afterward. It was a surprise to me that nodules occurred as the infection was subsiding. My associates and I had come to look on nodules as an evidence of rheumatic carditis whether this was visible clinically or not. In my own experience, the patients who had nodules did not usually show subsidence clinically, as far as the carditis was concerned, for some time afterward.

In a great many of these cases, the condition seemed to run a subacute course for a long time but with progressive damage to the heart. I should like to know what happened to these patients afterward in that regard.

Dr. Frederic W. Schlutz, Chicago: I should like to corroborate the experience which Dr. Struthers and Dr. Bacal had with reference to the advisability of tonsillectomy in these cases.

In the clinic of the Bobs Roberts Memorial Hospital for Children my associates and I favor tonsillectomy and removal of focal infection at as early a date as possible. We have been definitely under the impression that it is unwise to do this with a rising sedimentation rate and have found, in agreement with the experience of Dr. Struthers and Dr. Bacal, that recovery was sometimes delayed

I should like to voice the same surprise that the last speaker expressed that nodules appear in association with a falling sedimentation rate. My co-workers and I have had the opportunity to observe a great deal of rheumatism in Chicago, more than I encountered in Minnesota, and always had the impression that the onset of rheumatic nodules presaged an unfavorable change in the condition.

DR. HUGH MCCULLOCH, St. Louis: I should like to emphasize, as Dr. Struthers pointed out, the great need of having some method for knowing when the rheumatic infection has become inactive and the prognosis is favorable or when signs of return of rheumatic activity appear. Such a method as this, which might be called objective, will add to the methods already at the disposal of the physician.

For a long time we have been using the basal pulse rate, the basal temperature and gain in weight as the most useful guides for recognizing this terminal point of activity. These signs, too, are largely objective but of a different kind. Such a method as this will add greatly to the ability to recognize this point.

My associates and I have been using the sedimentation rate for some time at the St. Louis Children's Hospital, first, as a study for the accurate diagnosis of rheumatic fever and, more recently, to follow patients in the course of this disease. We believe that it is a satisfactory method to use in following the course of the rheumatic process but is not a useful sign of the disease itself.

There are two or three points which I would like to mention in order to ask Dr. Struthers some questions. First, about the patient who had chorea and who showed no change in the sedimentation rate. We believe that it is necessary to classify chorea properly, for a large number of the patients apparently do not have rheumatism as a basis for the chorea. There are a large number who show choreiform movements as a result of emotional instability, internal glandular disorders and, possibly, old encephalitis. It may be that some of the patients with chorea whom Dr. Struthers and Dr. Bacal observed who showed no change in the sedimentation rate may not have had rheumatic encephalitis.

Second, I should like to emphasize again the great importance of tonsillectomy in rheumatic subjects. These children do not respond to tonsillectomy in the way that ordinary children do, so that many extra precautions must be taken when this operation is performed on them. Is the sedimentation rate affected by tonsillectomy alone in these subjects?

I was interested to hear that such children usually require from four to six weeks to recover from this operation. That has been our experience.

Third, in our opinion, nodules in the rheumatic child mean that the patient is getting better. The disease may be getting worse, but the tissues are showing more response, and the ability to respond is a favorable sign. We would prefer that a patient very sick with rheumatic fever have rheumatic nodules rather than not have them.

DR. MAX SEHAM, Minneapolis: May I ask two questions? First, what are the results of the sedimentation test in infections of the upper respiratory tract and in other diseases, such as scarlet fever? Second, have the authors had any experience with the use of this test in afebrile, so-called muscular rheumatism?

DR. R. R. STRUTHERS, Montreal, Canada: I should like to express my gratitude to the various members who discussed this paper. I hoped that it would call forth some discussion.

I am afraid that a great many of the questions are beyond my ability to answer; the questions as to the various physical factors that affect the sedimentation rate, I am not prepared to discuss. Dr. Weech's observation that the sedimentation tends to rise before the appearance of fresh outbursts of activity is, I think, well recognized. That has been commented on by Schlesinger in his paper on "miniature rheumatic fever," in which the sedimentation rate tends to rise before the appearance of clinical reactivity.

As to Dr. Hart's question in connection with the end-results in the patients with nodules, these may appear during the course of the fall in the sedimentation rate. We have not followed the patients sufficiently long to give a definite answer, but our impression is that the children do not do as badly because of the presence of nodules as we had been previously taught. Heart disease is not necessarily more severe than in a child in whom nodules do not develop. I do not believe that they mean an unfavorable prognosis.

Schlesinger reported 25 cases in which nodules appeared during the course of the subsidence of the infection as judged by the sedimentation rate and expressed the opinion that they do not necessarily prognosticate severe carditis. We are familiar with the dangers of tonsillectomy in this disease, having unfortunately had one or two experiences with children on whom tonsillectomy was performed before the sedimentation rate was allowed to remain normal for at least a minimum period of six weeks. The sedimentation rate rose sharply, with evidence of recrudescence of the infection, and three to four months were required for it to return to normal. We regard the basic period of six weeks as being essential before operative intervention.

I am particularly grateful to Dr. McCulloch for his comment on nodules. My first introduction to nodes and rheumatism was made by Dr. McCulloch, of St. Louis, some fifteen years ago. In Montreal we have seen a great deal of rheumatism. This report covers 250 cases, and nodules were comparatively common.

I have not yet achieved the frame of mind of Dr. McCulloch, who would rather see a patient with nodules than without, although we do not regard nodules as being necessarily of serious import.

I agree that there are probably at least two types of chorea, one which follows rheumatic infection and one which apparently follows other infections or which follows emotional states. I do not know of any clinical method by which one can differentiate these two groups. We have come to the conclusion that one group of patients perhaps can return to school after the subsidence of their symptoms without necessarily having an immediate recurrence of chorea.

Unfortunately, we see a large number of children who are discharged as apparently well but who after a month at school return with evidence of chorea but no other evidence of rheumatic infection, such as rheumatic carditis.

I said that there are two groups of chorea. One can follow some patients for a period of years and note that carditis does not develop in those in whom chorea is not due to rheumatic infection. We have had under observation children with as many as four or five attacks of clinical chorea but in whom cardiac disease did not develop. It may be that those children belong to the group of which Dr. McCulloch spoke, in whom the chorea is not due to rheumatic disease.

In answer to Dr. Seham, the effect of infection of the upper respiratory tract on the sedimentation rate is apparently a question of degree. In cases in which fever is present with the infection of the upper respiratory tract there is usually an effect on the sedimentation rate, which is increased. Those children who have vague indefinite pains and so-called muscular rheumatism frequently show no effect in regard to the sedimentation rate; that cannot be stated dogmatically, but one sees children with the complaint of indefinite muscular pain who do not show alteration of the sedimentation rate.

FIVE CASES OF LYMPHOCYTIC CHORIOMENINGITIS IN MAN. DR. THOMAS M. RIVERS, New York, and T. F. MCNAIR SCOTT, M.R.C.P. (by invitation), London.

Lymphocytic choriomeningitis is the name applied to a disease of the nervous system in man lately recognized as due to a specific virus. We have been able to isolate the virus from the spinal fluid of 5 patients and from the blood of 1 of them.

The clinical pictures presented by these patients were similar. A prodromal illness, resembling influenza, was common to all; in 4 of them a severe headache associated with nausea or vomiting was the outstanding feature; in the fifth the onset was insidious, with stiffness of the neck and back culminating in a convulsion. The physical findings on admission were mainly those of mild meningeal irritation, namely, fever and stiff neck. Mental confusion and transient alterations of reflexes and in sensation were also observed. The leukocyte count was not abnormal. The spinal fluid of each patient contained an excess of lymph-

ocytes, an increased amount of protein and a somewhat diminished sugar content; it was sterile on ordinary bacteriologic mediums but when inoculated into mice and guinea-pigs produced a transmissible illness. Recovery appears to be complete in 4 of the patients, while the fifth is still under observation.

The characteristic signs of illness can be produced in the mouse by intracerebral inoculation of infectious material. These are irritability with clonic convulsions; death occurs in from 60 to 70 per cent of the animals. In the guinea-pig, inoculation by the intracerebral, the intranasal or the subcutaneous route produces fever, emaciation and labored breathing without frank neurologic signs. The rhesus monkey can be infected and responds, after an incubation period of from three to eight days, with fever, muscular stiffness and tremors; death or recovery results within three weeks.

The pathologic changes are noted mainly in the brain, spinal cord and lungs in all three hosts. The outstanding features are, in the mouse, a round cell meningeal reaction; in the guinea-pig, interstitial pneumonia with but slight meningeal involvement, and, in the monkey, round cell involvement of the meninges and the choroid plexuses. Because of this last feature Armstrong and Lillie, when they first isolated the virus from the brain of a monkey in 1934, gave the disease the present name.

Shortly after Armstrong and Lillie's findings, Traub, at Princeton, found a virus of similar nature among his stock white mice. At the same time we isolated the virus from the spinal fluid of the first 2 patients whose cases are reported here. By means of cross-reinoculation and cross-neutralization tests it was possible to show that all three viruses were the same.

By means of a neutralization test we were able to show that in 3 of our 5 patients tested neutralizing antibodies against the virus developed following their illness. Among thirty-three serums from patients suffering from a similar meningeal illness we have been able to find only four with neutralizing antibodies. Since in all such cases the condition falls under the clinical diagnosis of acute aseptic meningitis, we believe that this clinical syndrome has no single etiologic factor.

Lymphocytic choriomeningitis can be diagnosed as a routine by inoculating spinal fluid subcutaneously into a guinea-pig. If the results are positive the animal will show a characteristic illness that is transmissible to other pigs.

It is possible that some of the unexplained meningeal reactions in children are due to this virus.

DISCUSSION

Dr. Béla Schick, New York: I believe that there are different forms of this peculiar picture of lymphocytic meningitis. I had the opportunity to observe last year in Paris 2 cases in the clinic of Professor Debré. He had observed 5 more cases, and since that time new cases have been discovered. The patients showed high agglutination for the spirochete of Weil.

The children showed acute meningeal signs (vomiting, stiff neck, a positive Kernig sign, etc.) and a high temperature in the beginning. The prognosis was good, and recovery occurred in a relatively short time. Debré found that the disease could be transmitted to guinea-pigs.

It was interesting to see that the infection took place during the summer when the children were bathing in small rivers near Paris. It is possible that similar cases may occur in the United States and in Canada.

Dr. Joseph Stokes Jr., Philadelphia: I was much interested in the discussion of the paper by Dr. Rivers and Dr. Scott because of the fact that in Philadelphia, at the end of last summer, there was an epidemic of what might be termed aseptic meningitis or lymphocytic meningitis, which was studied rather carefully at the Philadelphia General Hospital and the Children's Hospital. In this group of cases there was one death. The material was transferred to monkeys and mice. No virus was isolated.

Dr. Scott examined the serum from these children and after followng them for two months, which is the time at which neutralizing properties appear in choriomeningitis, he found none. A few cases of poliomyelitis were reported in the

city at that time, and the question arose as to whether this condition might not be poliomyelitis. Although little virus appeared in the spinal fluid, the fact that injections of spinal fluid from several patients and emulsions of the cord of the child who died did not result in poliomyelitis suggests that this disease was not responsible for the epidemic.

In other words, my associates and I could find no etiologic agent for this disease, and it corresponds with a large group of lymphocytic or aseptic meningitis that Dr. Schick has mentioned.

It seems to me that physicians owe a great deal to Dr. Rivers, Dr. Scott, Dr. Armstrong and Dr. Lillie for the separation of this disease entity from the conglomerate group termed aseptic meningitis.

PRESENCE OF THE MENINGOCOCCUS IN THE NASOPHARYNX OF NORMAL PERSONS. DR. NELLES SILVERTHORNE, Toronto, Canada.

The nasopharynges of approximately 50 normal healthy adults were swabbed monthly for a period of two years. From 16 to 28 per cent of these persons were found to be harboring the meningococcus. The virulence of the strains was studies. The bactericidal effect of samples of human blood, especially of samples of the carriers' blood, on the respective strains and on strains from the cerebrospinal fluid was investigated.

DISCUSSION

DR. JAMES DOWLING TRASK, New Haven, Conn.: How do you explain the high incidence of positive carriers? Did you use special mediums? My associates and I use fresh blood agar plates, and it is unusual to find carriers of meningococci in the wards for patients with infectious disease of the New Haven Hospital.

DR. HENRY F. HELMHOLZ, Rochester, Minn.: I am greatly interested in Dr. Silverthorne's results. My associates and I have found that in southern Minnesota meningococcic meningitis is sporadically present. In a recent outbreak one child died within six hours. A second apparently had the same infection, but at the time it entered the hospital it had an almost normal temperature but a positive blood culture. On taking cultures from members of the families in this locality we found that the father and mother, one other sister and an uncle had cultures from the throat that were positive for the meningococcus. Twelve persons on surrounding farms had negative cultures. We made cultures from the same persons two weeks later and found that all the cultures were negative.

We have been using the method that Thompson has suggested, in which the meningococcus is grown in an atmosphere of carbon dioxide. Within from twelve to twenty-four hours the meningococcus grows in large colonies. The same technic has been applied successfully to the growth of the gonococcus.

DR. NELLES SILVERTHORNE, Toronto, Canada: In answer to the first question, I have found there is really no "trick" in getting a high percentage of carriers. One merely has to use a direct swab in the nasopharynx, spread the material on the blood agar plate and incubate it for twenty-four hours. We have found that all these meningococci fulfil the various tests for the meningococcus microscopically, culturally and serologically.

URINARY ALKALINITY IN YOUNG CHILDREN AS INFLUENCED BY DIET AND DISEASE. DR. FRANK C. NEFF, DR. ROBERT C. FREDEEN (by invitation), DR. DAVID T. LOY (by invitation) and DR. GEORGE V. HERRMAN (by invitation), Kansas City, Mo.

For alkalinizing the urine therapeutically, base-forming elements in the diet are well used instead of drugs. It is known that adults can take unlimited quantities of orange juice without showing any tendency toward acidosis, and this is equally true of children.

We are interested in the clinical significance of alkaline states of the urine in early life. This paper deals with the study of the p_H, especially in the higher levels, and the relationship not only to the dietary but to certain diseases.

The p_H of the urine of a series of new-born infants was studied as influenced by the usual amounts of breast milk or mixed feeding in the obstetric nursery. The determinations of the p_H were made by the electrometric method.

As a summary of the findings in the new-born infants, it was seen that the level of the p_H is in the acid zone, usually from 5.8 to 6.3. There is little difference in the acidity whether the infant is on breast milk, bottle milk or mixed feeding. Lactic acid milk alone produces a p_H which is usually a few decimals lower than that produced by breast milk alone.

It seems to us reasonable to feed sufficient quantities of base-forming fruit and vegetable juices as a substitute for alkalinizing drugs or as an adjuvant. These juices may be given in quantities large enough to replace some of the milk with its high acid-forming protein.

Young children with chronic pyuria usually have an alkaline urine. The p_H of the urine of a child with urinary infection due to Bacillus proteus was studied for several months. This child was often in a state of renal acidosis, incapable of excreting an acid urine. Feeding a ketogenic diet precipitated acidosis, but the child was greatly benefited by large amounts of base-forming fruit juice.

Studies of 5 older children on an unrestricted diet, a restricted diet or a high protein diet showed that more orange juice than grape juice is required to neutralize the acidity of the urine.

An application of the knowledge regarding the composition of the urine as affected by the excess of base or acid in the diet is of great value in the treatment of children.

MANDELIC ACID IN THE TREATMENT OF URINARY INFECTIONS. DR. HENRY F. HELMHOLZ, Rochester, Minn.

The difficulties of administering the ketogenic diet make the replacements of beta-oxybutyric acid by mandelic acid, as suggested by Rosenheim, of great value. Excreted unchanged in the urine, mandelic acid has bactericidal properties closely resembling those of beta-oxybutyric acid. It is readily taken and only occasionally gives rise to nausea and diarrhea. Hematuria has been described as a result of its administration, but I have not encountered it in any of my cases.

The concentration and p_H at which mandelic acid acts bactericidally vary for different organisms. A series of ten strains of colon bacilli, ten of Aerobacter, five of Proteus and five of Pseudomonas were tested. The proteus organisms were most easily killed. Thirteen strains of Escherichia coli were killed in a 0.25 per cent dilution of mandelic acid at p_H 5.0, in a 0.5 per cent dilution of the acid at p_H 5.3 and in a 1.0 per cent dilution at p_H 5.7. The aerobacter and pseudomonas groups varied in their resistance to the drug; a minority responded in the same range as the colon group of organisms did, whereas seven of the strains of Aerobacter and three of those of Pseudomonas required a higher concentration of acid and a lower p_H of the urine to kill them. This variation accounts for the difficulty in ridding some patients of infection. Staphylococci seem to react in the same manner as the bacillary organisms.

At the Mayo Clinic my associates and I have used mandelic acid clinically in the treatment of urinary infections and prophylactically in the treatment of patients who had to undergo operation on the urinary passages in the presence of obstruction. We have also used it in 3 cases in which we were able to obtain separate specimens of urine from each kidney in order to get information as to the difference between the output of the normal kidney and that of the diseased kidney.

In 2 of 4 cases of pyelitis without any anomaly in the urinary tract the condition was of long duration; in the other 2 cases it was of unknown duration. One patient, a boy suffering from cerebral palsy, was in the hospital for treatment of pneumonia when the pyelitis was discovered. An infection due to Streptococcus faecalis cleared up rapidly but recurred during the following week; it yielded again to treatment and has not recurred since. Each of 2 girls had an infection due to Escherichia coli, of long duration—ten years in the one case and seven

in the other. In the latter instance the infection had resulted in cystitis cystica. The former patient had had several relapses until a small amount of redundant tissue was removed by cautery from the neck of the bladder. The fourth patient's infection cleared up rapidly after removal of a hydronephrotic kidney.

There were 6 cases of urinary anomalies in which the patients were treated by means of mandelic acid. A cure was obtained in 3 cases; treatment failed in 2 cases, and in the remaining case a relapse occurred after two months. One patient, a girl of 13 years, has had the infection since the second day of her life and for the first time now has had a sterile urine. She has been treated on numerous occasions by the most approved methods at our disposal, but previously without any effect.

As compared with the normal kidney, the diseased kidney excretes urine of a higher p_H and lower concentration of mandelic acid. Thus the usefulness of the drug in the treatment of patients with seriously damaged kidneys is limited.

In two cases of obstruction of the neck of the bladder, with distention of the bladder above the umbilicus, suprapelvic cystotomy and transurethral resection were performed, without any resulting rise in the temperature or the presence of bacillary organisms in the urine during a perod of three weeks.

The ease of administration of mandelic acid and the constant bactericidal effect on all the organisms studied make it a useful agent in the treatment of urinary infections and in the prevention of infection during operations on the urinary tract.

DISCUSSION

Dr. Kenneth D. Blackfan, Boston: Dr. Dietrich, at our clinic at the Children's Hospital, has been studying the effect of sodium mandelate in infections of the genito-urinary system for the past year, and I wish to confirm the observations of Dr. Helmholz by reporting similar results on 16 patients.

The treatment of the small child is somewhat difficult because of the unpleasantness of the remedy. I am wondering whether Dr. Helmholz has had any experience with the use of ammonium mandelate, as recently suggested by one of the English writers.

Another point which has been of some interest to my associates and me is the reaction which we observed, I think, in 2 patients. That is an increased amount of albumin, white cells and red cells. These findings subsided as soon as the treatment was discontinued.

Dr. L. Emmett Holt Jr., Baltimore: The experience of my associates and me in Baltimore has been confined to 2 patients, both of whom have been treated with ammonium mandelate as recently reported by British workers. The ammonium mandelate can be made into a palatable elixir, and no difficulty in administration was encountered. In one case the result was not satisfactory. In the second case red cells and casts in the urine developed in a day or two, and the treatment was therefore discontinued. This confirms the experience from Dr. Blackfan's clinic and of the British workers that the treatment may cause renal irritation.

Dr. Alfred T. Shohl, Mirror Lake, N. H.: I should like to ask Dr. Helmholz a question: As the bactericidal power of this and similar compounds is closely related to the p_H and hence must be related to the strength of the acid used and the amount of free acid present (the greater the increase in p_H and the greater the amount of free acid present the greater the bactericidal power), would it not simplify matters if instead of expressing the reaction in terms of both p_H and, as I understand it, the total amount of mandelic acid present, one were to express it more simply in the amount of free acid effective in preventing the growth of bacteria?

Dr. Franklin Paul Gengenbach, Denver: I should like to ask Dr. Helmholz whether he always uses ammonium chloride with the mandelic acid.

Dr. Henry F. Helmholz, Rochester, Minn.: My associates and I have used ammonium mandelate in one case. We have not had difficulty in getting children to take it. I have taken a dose as large as 5 Gm., without any ill effects. If it

is taken immediately after meals I do not believe that it is likely to cause vomiting, although in one case we did have difficulty in getting the patient to take it in preparation for an operation on a hydronephrotic kidney. I think that it will probably be possible to give this preparation in a much more palatable form than that we are using at the present time.

When one sees a child who will take 1 and even 2 Gm. of ammonium chloride four times a day one realizes that some of the doses of ammonium chloride that one is accustomed to give are rather small.

In our series of cases we have not seen hematuria. We have been looking for it because in the original article this was given as one of the contraindications. We have seen in a patient with bilateral marked dilatation of the ureter and a blood urea content of about 60 mg. per hundred cubic centimeters after four days of the administration of mandelic acid, without a change in the urinary findings, a blood urea content which mounted to 120 mg. per hundred cubic centimeters and fell within a week to almost the original figure.

We have also shown experimentally in dogs that when this acid is administered intravenously there is a marked reduction in the urea clearance, which returns to normal after a relatively short period. There is no question that mandelic acid can do harm to the kidney, particularly to an injured kidney, but I believe that the factor of safety is such that it can be very useful in the treatment of urinary infection.

I am sorry that I am not enough of a chemist to answer Dr. Shohl's question.

(To be Concluded)

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Heereplein, Groningen, The Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

FOREIGN

British Paediatric Association

President: Dr. Leonard Findlay, 14 Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Sir Lancelot Barrington-Ward, 85 Harley St., London, W. 1.
Secretary: Dr. K. H. Tallerman, 122 Harley St., London, W. 1.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:30 p. m.

Paediatrický Spolok na Slovensku

President: Dr. A. J. Chura, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

Sociedad Cubana de Pediatría

President: Prof. Félix Hurtado Galtés, Carlos III, 7, Havana.
Secretary: Dr. Carlos Hernández Miyares, San Lazaro 370, Havana.
Place: Cátedra de Clínica Infantil, Hospital Mercedes, Havana. Time: Third Thursday of every month.

Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv, Palestine.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv, Palestine.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Ralph M. Tyson, 255 S. 17th St., Philadelphia.
Secretary: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Place: Atlantic City, N. J. Time: June 7-11, 1937.

American Academy of Pediatrics

President: Dr. Laurence R. DeBuys, 1417 Delachaise St., New Orleans, La.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: Waldorf-Astoria Hotel, New York: Time: June 3, 4 and 5, 1937.
Region I. Place: Belvedere Hotel, Baltimore. Time: Nov. 16 and 17, 1936.
Region II. Place: Belvedere Hotel, Baltimore. Time: Nov. 16 and 17, 1936.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

AMERICAN HOSPITAL ASSOCIATION, CHILDREN'S HOSPITAL SECTION

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Fritz B. Talbot, 270 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. A. P. Hart, 1844 Bloor St., W., Toronto, Ont.
Secretary-Treasurer: Dr. Pearl Summerfeldt, Hospital for Sick Children, Toronto, Ont.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. Francis Scott Smyth, University of California Medical School, San Francisco.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

SECTIONAL

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. L. Howard Smith, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. Morris Bridgeman, Children's Clinic, Portland, Ore.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON PEDIATRICS

Chairman: Dr. Madison Hines Roberts, 104 Ponce de Leon Ave., N. E., Atlanta, Ga.
Secretary: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. J. W. Britton, 931 Noble St., Anniston.
Secretary-Treasurer: Dr. Wallace Clyde, Employees' Hospital, Fairfield.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. A. C. Kirby, 701 Main St., Little Rock.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary: Dr. E. Earl Moody, 3780 Wilshire Blvd., Los Angeles.

FLORIDA STATE PEDIATRIC SOCIETY

President: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville.
Secretary: Dr. Warren W. Quillian, 227 Avenue Aragon, Miami.
Place: Concurrent with state association meeting at time of convention.

GEORGIA PEDIATRIC SOCIETY

President: Dr. Mercer Blanchard, 1301 Broadway, Columbus.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St., N. E., Atlanta.
Place: Atlanta. Time: December 1936.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. Milo K. Miller, 122 N. Lafayette Blvd., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. Edwin A. Socola, 2000 Tulane Ave., New Orleans.
Secretary-Treasurer: Dr. Ruth Aleman, 1407 S. Carrollton Ave., New Orleans.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. George M. Retan, 459 James St., Syracuse.
Secretary: Dr. John D. Craig, 33 E. 61st St., New York.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Harvey F. Garrison, 319 E. Capitol Pl., Jackson.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Leroy J. Butler, 405 N. Spring St., Winston-Salem.
Secretary: Dr. C. A. Street, 405 N. Spring St., Winston-Salem.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Julian Feild, 610 S. Monroe St., Enid.
Secretary: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.

PENNSYLVANIA MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Joseph Stokes, Children's Hospital, Philadelphia.
Secretary: Dr. Theodore O. Elterich, 310 Medical Arts Bldg., Pittsburgh.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Leland B. Salters, 317 S. Warley St., Florence.
Secretary-Treasurer: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.

TEXAS PEDIATRIC SOCIETY

President: Dr. George B. Cornick, 507½ E. Houston St., San Antonio.
Secretary-Treasurer: Dr. F. H. Lancaster, 1507 Medical Arts Bldg., Houston.
Place: Houston. Time: Fall, 1936.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Basil B. Jones, 1028 W. Franklin St., Richmond.
Secretary: Dr. W. A. McGee, 616 W. Grace St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. John T. Thornton, 58, 16th St., Wheeling.
Secretary: Dr. Claude L. Holland, 400 Locust Ave., Fairmont.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. D. Pilcher, City Hospital, Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. T. B. Verner, 170 St. George St., Toronto.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto.

BRONX PEDIATRIC SOCIETY

President: Dr. Harry D. Pasachoff, 1560 Grand Concourse, New York.
Secretary: Dr. Samuel Tripler, 1555 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. Thurman B. Givan, 115 Remson St., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vasder Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Robert Black, Del Prado Hotel, Chicago.
Secretary: Dr. James H. Wallace, 715 Lake St., Oak Park, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

DALLAS PEDIATRIC SOCIETY

President: Dr. I. T. Nesbitt, 1719 Pacific Ave., Dallas, Texas.
Secretary: Dr. John E. Ashby, 3622 Fairmount Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

DETROIT PEDIATRIC SOCIETY

President: Dr. Edward A. Wishropp, 10 Peterboro St., Detroit.
Secretary: Dr. W. J. Scott, 5140 Second Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

FULTON COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (ATLANTA, GA.)

Chairman: Dr. Joseph Yampolsky, 478 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. H. W. Brayton, 179 Allyn St., Hartford.
Secretary: Dr. Ernest Caulfield, 683 Asylum Ave., Hartford.

Houston Pediatric Society

President: Dr. E. O. Fitch, 3717 Main St., Houston, Texas.
Secretary-Treasurer: Dr. Fred Ames, Medical Arts Bldg., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Intermountain Pediatric Society

President: Dr. Eugene Smith, 385 Twenty-Fourth St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1103 Grand Ave., Kansas City.
Secretary: Dr. S. A. Stadler, 6133 Brookside Blvd., Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. George P. Laton, 1136 W. 6th St.
Secretary-Treasurer: Dr. Edwin F. Patton, 3875 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Harry Apfel, 988 Park Pl., Brooklyn.
Secretary: Dr. Max Palinsky, 1270, 45th St., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. W. C. A. Steffen, 42 Union St., Flushing, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144, 38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Memphis Pediatric Society

President: Dr. W. D. Mims, 1042 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. R. Graves, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month, except June, July and August, 8 p. m.

Milwaukee Pediatric Society

President: Dr. J. Gurney Taylor, 324 E. Wisconsin St., Milwaukee.
Secretary: Dr. H. B. Miner, 425 E. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Paul Emerson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Henry E. Gallup, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Béla Schick, 17 E. 84th St., New York.
Secretary: Dr. Alexander T. Martin, 107 E. 85th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. A. V. Stoesser, University Hospital, Minneapolis.
Secretary: Dr. Roger L. J. Kennedy, Mayo Clinic, Rochester, Minn.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Philadelphia Pediatric Society

President: Dr. H. H. Perlman, 1904 N. Franklin St., Philadelphia.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. James LeRoy Foster, Highland Bldg., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200 Fifth Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. W. E. Chapin, 1001 E. Clay St., Richmond, Va.
Secretary-Treasurer: Dr. Emily Gardner, 1100 W. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

Rochester Pediatric Society

President: Dr. F. W. Bush, 29 N. Goodman St., Rochester, N. Y.
Secretary: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

Rocky Mountain Pediatric Society

President: Dr. Ralph Verploeg, 1850 Gilpin St., Denver.
Secretary: Dr. Max M. Ginsburg, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. John Zahorsky, 536 N. Taylor Ave., St. Louis.
Secretary-Treasurer: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. Arthur E. Wade, 1215, 4th Ave., Seattle.
Secretary: Dr. Walter B. Seelye, Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Secretary: Dr. Philip E. Rothman, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Samuel Levin, 2501 W. Grand Blvd., Detroit.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (NEW YORK)

President: Dr. Louis V. Waldron, 149 N. Broadway, Yonkers, N. Y.
Secretary-Treasurer: Dr. Fairfax Hall, 421 Huguenot St., New Rochelle, N. Y.
Place: Grasslands Hospital. Time: Third Thursday, Oct., Dec., Feb. and April